Figure 1
Sequence of human APRIL (SEQ ID NOS: 1 and 2)

Human G70 cDNA (SEQ ID NO 1)

Length: 1465 bp

```
     1  GCCAACCTTC CCTCCCCCAA CCCTGGGGCC GCCCCAGGGT TCCTGCGCAC
    51  TGCCTGTTCC TCCTGGGTGT CACTGGCAGC CCTGTCCTTC CTAGAGGGAC
   101  TGGAACCTAA TTCTCCTGAG GCTGAGGGAG GGTGGAGGGT CTCAAGGCAA
   151  CGCTGGCCCC ACGACGGAGT GCCAGGAGCA CTAACAGTAC CCTTAGCTTG
   201  CTTTCCTCCT CCCTCCTTTT TATTTTCAAG TTCCTTTTTA TTTCTCCTTG
   251  CGTAACAACC TTCTTCCCTT CTGCACCACT GCCCGTACCC TTACCCGCCC
   301  CGCCACCTCC TTGCTACCCC ACTCTTGAAA CCACAGCTGT TGGCAGGGTC
   351  CCCAGCTCAT GCCAGCCTCA TCTCCTTTCT TGCTAGCCCC CAAAGGGCCT
   401  CCAGGCAACA TGGGGGGCCC AGTCAGAGAG CCGGCACTCT CAGTTGCCCT
   451  CTGGTTGAGT TGGGGGGCAG CTCTGGGGGC CGTGGCTTGT GCCATGGCTC
   501  TGCTGACCCA ACAAACAGAG CTGCAGAGCC TCAGGAGAGA GGTGAGCCGG
   551  CTGCAGGGGA CAGGAGGCCC CTCCCAGAAT GGGGAAGGGT ATCCCTGGCA
   601  GAGTCTCCCG GAGCAGAGTT CCGATGCCCT GGAAGCCTGG GAGAGTGGGG
   651  AGAGATCCCG GAAAAGGAGA GCAGTGCTCA CCCAAAAACA GAAGAAGCAG
   701  CACTCTGTCC TGCACCTGGT TCCCATTAAC GCCACCTCCA AGGATGACTC
   751  CGATGTGACA GAGGTGATGT GGCAACCAGC TCTTAGGCGT GGGAGAGGCC
   801  TACAGGCCCA AGGATATGGT GTCCGAATCC AGGATGCTGG AGTTTATCTG
   851  CTGTATAGCC AGGTCCTGTT TCAAGACGTG ACTTTCACCA TGGGTCAGGT
   901  GGTGTCTCGA GAAGGCCAAG GAAGGCAGGA GACTCTATTC CGATGTATAA
   951  GAAGTATGCC CTCCCACCCG GACCGGGCCT ACAACAGCTG CTATAGCGCA
  1001  GGTGTCTTCC ATTTACACCA AGGGGATATT CTGAGTGTCA TAATTCCCCG
  1051  GGCAAGGGCG AAACTTAACC TCTCTCCACA TGGAACCTTC CTGGGGTTTG
  1101  TGAAACTGTG ATTGTGTTAT AAAAAGTGGC TCCCAGCTTG GAAGACCAGG
  1151  GTGGGTACAT ACTGGAGACA GCCAAGAGCT GAGTATATAA AGGAGAGGGA
  1201  ATGTGCAGGA ACAGAGGCGT CTTCCTGGGT TTGGCTCCCC GTTCCTCACT
  1251  TTTCCCTTTT CATTCCCACC CCCTAGACTT TGATTTTACG GATATCTTGC
  1301  TTCTGTTCCC CATGGAGCTC CGAATTCTTG CGTGTGTGTA GATGAGGGGC
  1351  GGGGGACGGG CGCCAGGCAT TGTTCAGACC TGGTCGGGGC CCACTGGAAG
  1401  CATCCAGAAC AGCACCACCA TCTAACGGCC GCTCGAGGGA AGCACCCGGC
  1451  GGTTTGGGCG AAGTC
```

The proposed transmembrane domains are boxed

human G70 protein sequence (SEQ ID NO 2)

```
     1  MPASSPFLLA PKGPPGNMGG PVREPALSVA LWLSWGAALG AVACAMALLT
    51  QQTELQSLRR EVSRLQGTGG PSQNGEGYPW QSLPEQSSDA LEAWESGERS
   101  RKRRAVLTQK QKKQHSVLHL VPINATSKDD SDVTEVMWQP ALRRGRGLQA
   151  QGYGVRIQDA GVYLLYSQVL FQDVTFTMGQ VVSREGQGRQ ETLFRCIRSM
   201  PSHPDRAYNS CYSAGVFHLH QGDILSVIIP RARAKLNLSP HGTFLGFVKL
```

Figure 2A
Sequence of mouse G70 (SEQ ID NOS: 3 and 4)

Mouse G70 (SEQ ID NO 3)

```
   1  CATGCCGAGT GCTTTGTGTG TGTTACCTGC TCTAAGAAGC TGGCTGGGCA
  51  GCGTTTCACC GCTGTGGAGG ACCAGTATTA CTGCGTGGAT TGCTACAAGA
 101  ACTTTGTGGC CAAGAAGTGT GCTGGATGCA AGAACCCCAT CACTGGGTTT
 151  GGTAAAGGCT CCAGTGTGGT GGCCTATGAA GGACAATCCT GGCACGACTA
 201  CTGCTTCCAC TGCAAAAAAT GCTCCGTGAA TCTGGCCAAC AAGCGCTTTG
 251  TATTTCATAA TGAGCAGGTG TATTGCCCTG ACTGTGCCAA AAAGCTGTAA
 301  CTTGACGGCT GCCCTGTCCT TCCTAGATAA TGGCACCAAA TTCTCCTGAG
 351  GCTAGGGGGG AAGGAGTGTC AGAGTGTCAC TAGCTCGACC CTGGGGACAA
 401  GGGGGACTAA TAGTACCCTA GCTTGATTTC TTCCTATTCT CAAGTTCCTT
 451  TTTATTTCTC CCTTGCGTAA CCCGCTCTTC CCTTCTGTGC CTTTGCCTGT
 501  ATTCCCACCC TCCCTGCTAC CTCTTGGCCA CCTCACTTCT GAGACCACAG
 551  CTGTTGGCAG GGTCCCTAGC TCATGCCAGC CTCATCTCCA GGCCACATGG
 601  GGGGCTCAGT CAGAGAGCCA GCCCTTTCGG TTGCTCTTTG GTTGAGTTGG
 651  GGGGCAGTTC TGGGGGCTGT GACTTGTGCT GTCGCACTAC TGATCCAACA
 701  GACAGAGCTG CAAAGCCTAA GGCGGGAGGT GAGCCGGCTG CAGCGGAGTG
 751  GAGGGCCTTC CCAGAAGCAG GGAGAGCGCC CATGGCAGAG CCTCTGGGAG
 801  CAGAGTCCTG ATGTCCTGGA AGCCTGGAAG GATGGGGCGA AATCTCGGAG
 851  AAGGAGAGCA GTACTCACCC AGAAGCACAA GAAGAAGCAC TCAGTCCTGC
 901  ATCTTGTTCC AGTTAACATT ACCTCCAAGG ACTCTGACGT GACAGAGGTG
 951  ATGTGGCAAC CAGTACTTAG GCGTGGGAGA GGCCTGGAGG CCCAGGGAGA
1001  CATTGTACGA GTCTGGGACA CTGGAATTTA TCTGCTCTAT AGTCAGGTCC
1051  TGTTTCATGA TGTGACTTTC ACAATGGGTC AGGTGGTATC TCGGGAAGGA
1101  CAAGGGAGAA GAGAAACTCT ATTCCGATGT ATCAGAAGTA TGCCTTCTGA
1151  TCCTGACCGT GCCTACAATA GCTGCTACAG TGCAGGTGTC TTTCATTTAC
1201  ATCAAGGGGA TATTATCACT GTCAAAATTC CACGGGCAAA CGCAAAACTT
1251  AGCCTTTCTC CGCATGGAAC ATTCCTGGGG TTTGTGAAAC TATGATTGTT
1301  ATAAAGGGGG TGGGGATTTC CCATTCCAAA AACTGGCTAG ACAAAGGACA
1351  AGGAACGGTC AAGAACAGCT CTCCATGGCT TTGCCTTGAC TGTTGTTCCT
1401  CCCTTTGCCT TTCCCGCTCC CACTATCTGG GCTTTGACTC CATGGATATT
1451  AAAAAAGTAG AATATTTTGT GTTTATCTCC CAAAAA
```

Figure 2B

Mouse G70 Length: 241 (SEQ ID NO 4)

```
  1  MPASSPGHMG GSVREPALSV ALWLSWGAVL GAVTCAVALL IQQTELQSLR
 51  REVSRLQRSG GPSQKQGERP WQSLWEQSPD VLEAWKDGAK SRRRRAVLTQ
101  KHKKKHSVLH LVPVNITSKD SDVTEVMWQP VLRRGRGLEA QGDIVRVWDT
151  GIYLLYSQVL FHDVTFTMGQ VVSREGQGRR ETLFRCIRSM PSDPDRAYNS
201  CYSAGVFHLH QGDIITVKIP RANAKLSLSP HGTFLGFVKL *
```

G-70 FLAG des92 (smuG70) Strain #4081 (SEQ ID NO 19):

```
MDYKDDDDKKHKKKHSVLHLVPVNITSKDSDVTEVMWQPVLRRGRGLEAQGDIVRVW
DTGIYLLYSQVLFHDVTFTMGQVVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAG
VFHLHQGDIITVKIPRANAKLSLSPHGTFLGFVKL*
```

Figure 3
Alignm. of human and mouse G70

```
mouse: 1   MPASS---------PGHMGGSVREPALSVALWLSWGAVLGAVTCAVALLIQQTELQSLRR 51
           MPASS          PG+MGG VREPALSVALWLSWGA LGAV CA+ALL QQTELQSLRR
Human: 1   MPASSPFLLAPKGPPGNMGGPVREPALSVALWLSWGAALGAVACAMALLTQQTELQSLRR 60

mouse: 52  EVSRLQRSGGPSQKQGERPWQSLWEQSPDVLEAWKDGAKSRRRRAVLTQKHKKKHSVLHL 111
           EVSRLQ +GGPSQ      PWQSL EQS D LEAW+ G +SR+RRAVLTQK KK+HSVLHL
human: 61  EVSRLQGTGGPSQNGEGYPWQSLPEQSSDALEAWESGERSRKRRAVLTQKQKKQHSVLHL 120

mouse: 112 VPVNITSKD-SDVTEVMWQPVLRRGRGLEAQGDIVRVWDTGIYLLYSQVLFHDVTFTMGQ 170
           VP+N TSKD SDVTEVMWQP LRRGRGL+AQG  VR+ D G+YLLYSQVLF DVTFTMGQ
human: 121 VPINATSKDDSDVTEVMWQPALRRGRGLQAQGYGVRIQDAGVYLLYSQVLFQDVTFTMGQ 180

mouse: 171 VVSREGQGRRETLFRCIRSMPSDPDRAYNSCYSAGVFHLHQGDIITVKIPRANAKLSLSP 230
           VVSREGQGR+ETLFRCIRSMPS PDRAYNSCYSAGVFHLHQGDI++V IPRA AKL+LSP
human: 181 VVSREGQGRQETLFRCIRSMPSHPDRAYNSCYSAGVFHLHQGDILSVIIPRARAKLNLSP 240

mouse: 231 HGTFLGFVKL 240
           HGTFLGFVKL
human: 241 HGTFLGFVKL 250
```

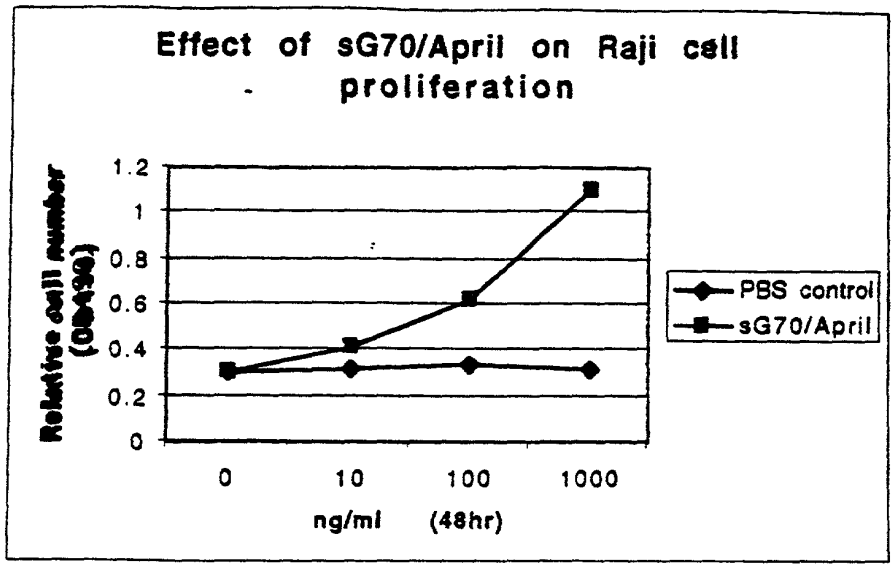
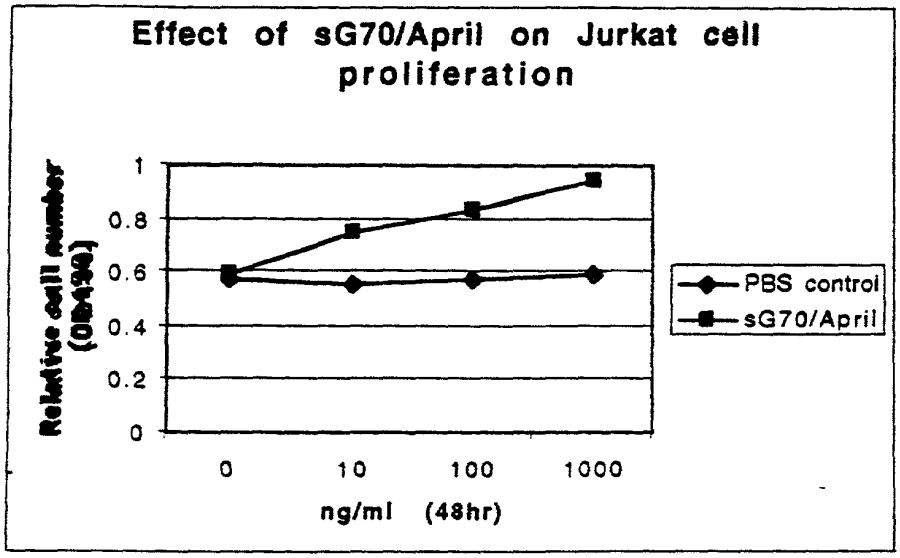


Fig. 4A



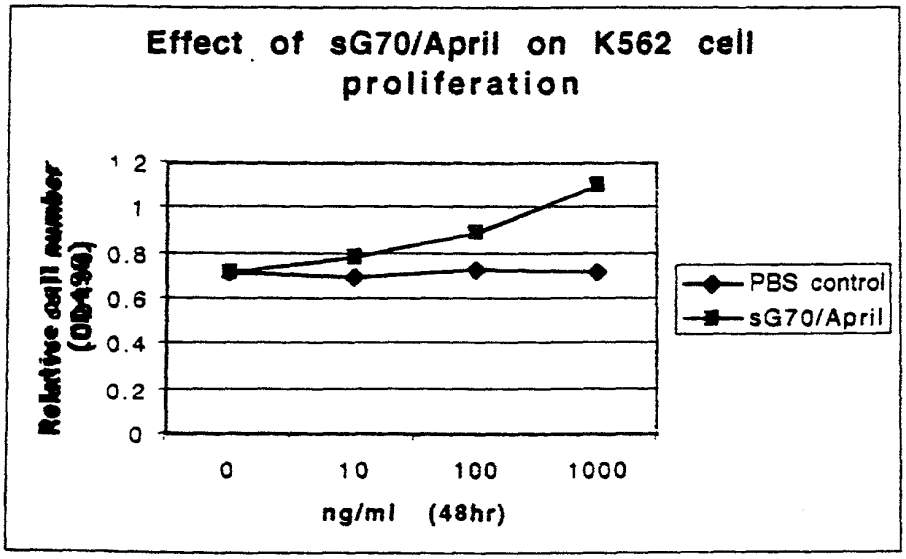
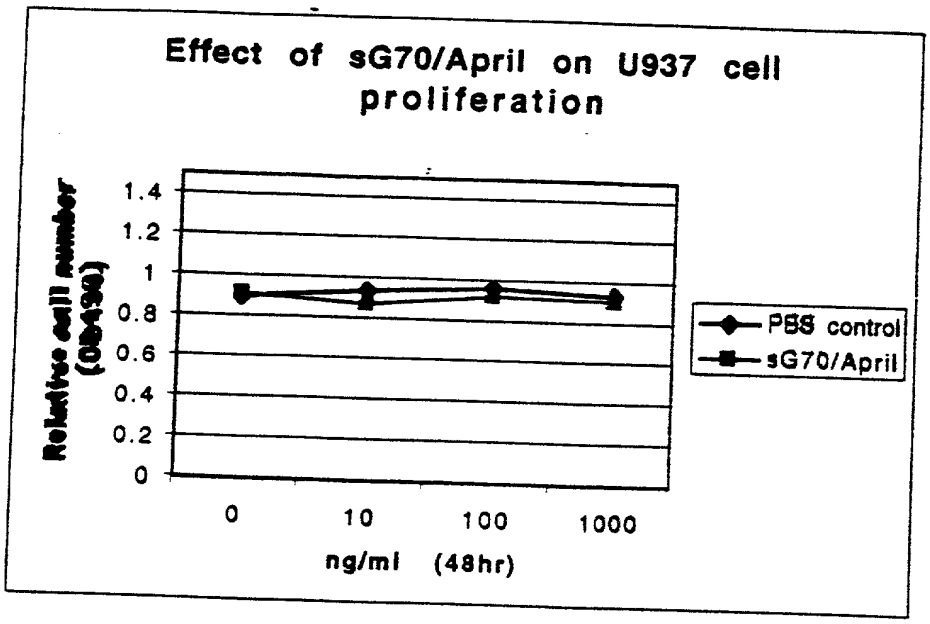
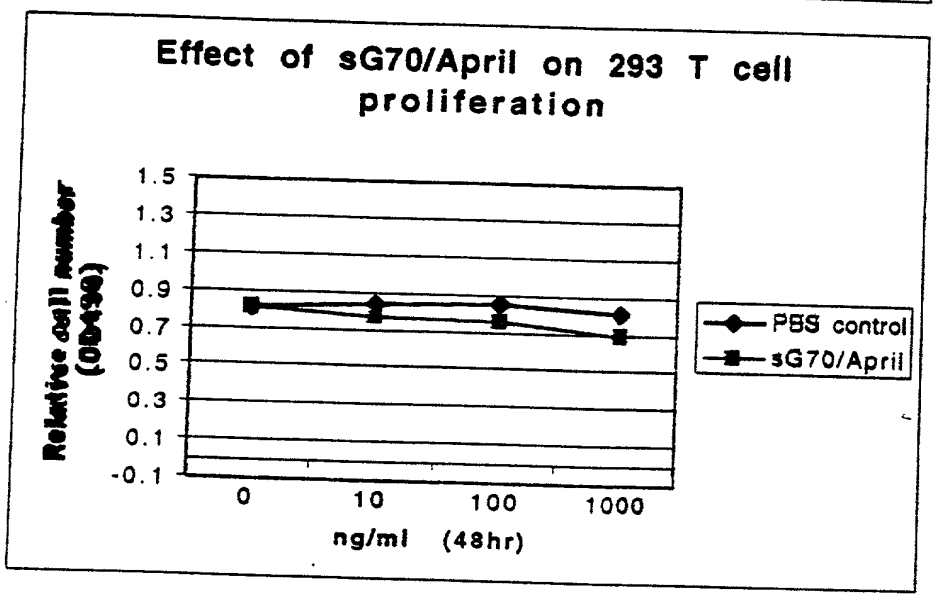


Fig. 4B


Effect of sG70/April on U937 cell proliferation
Relative cell number (OD490)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April


Effect of sG70/April on 293 T cell proliferation
Relative cell number (OD490)
1.5
1.3
1.1
0.9
0.7
0.5
0.3
0.1
-0.1
0
10
100
1000
ng/ml (48hr)
PBS control
sG70/April

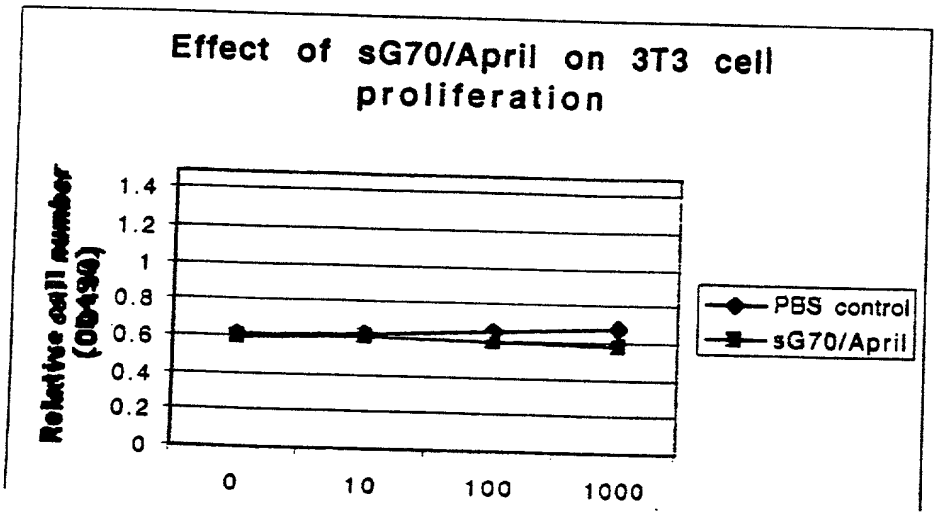
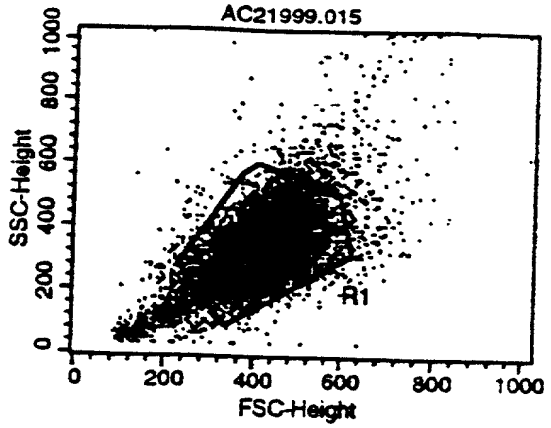
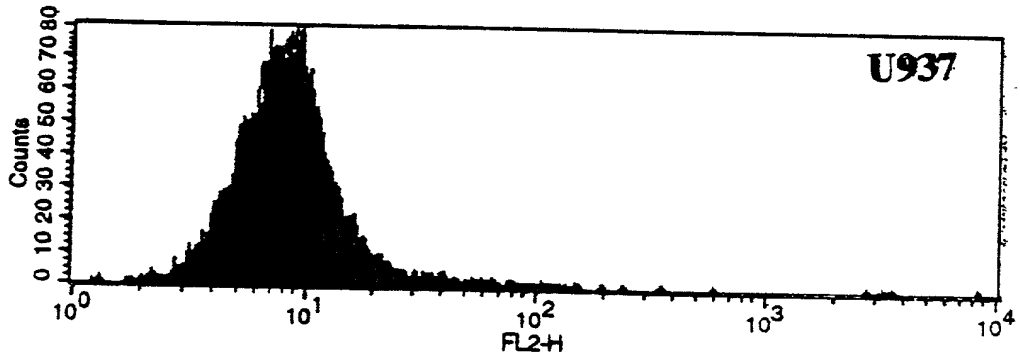
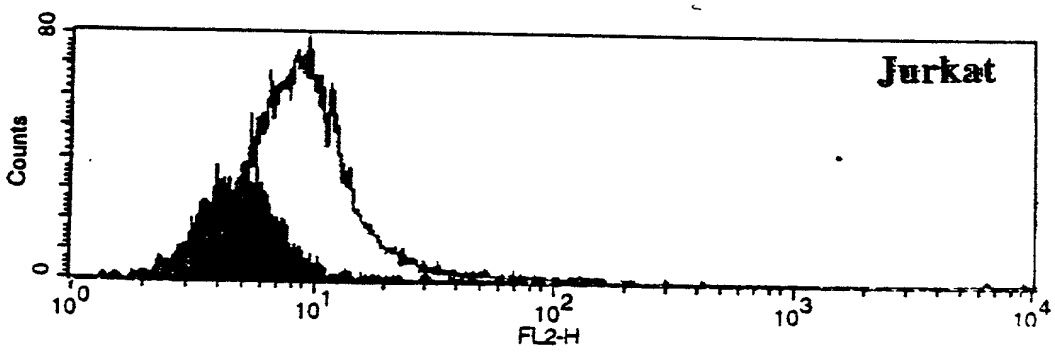

Effect of sG70/April on 3T3 cell proliferation
Relative cell number (OD490)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
PBS control
sG70/April

FIGURE 5A



FACS analysis of G70/April receptor binding





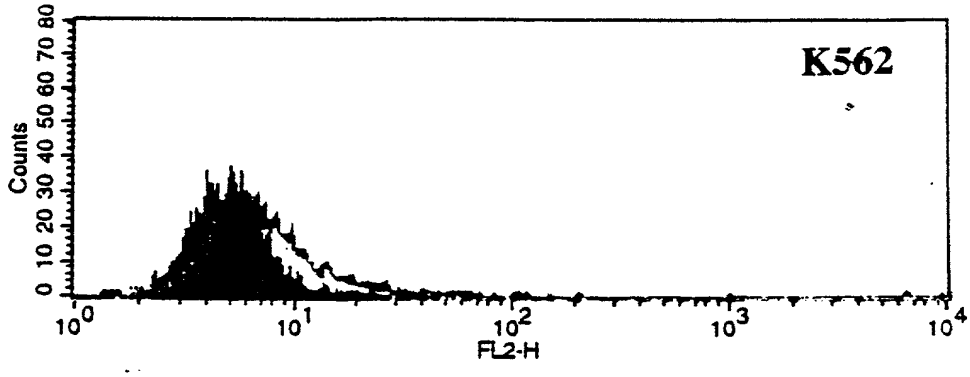
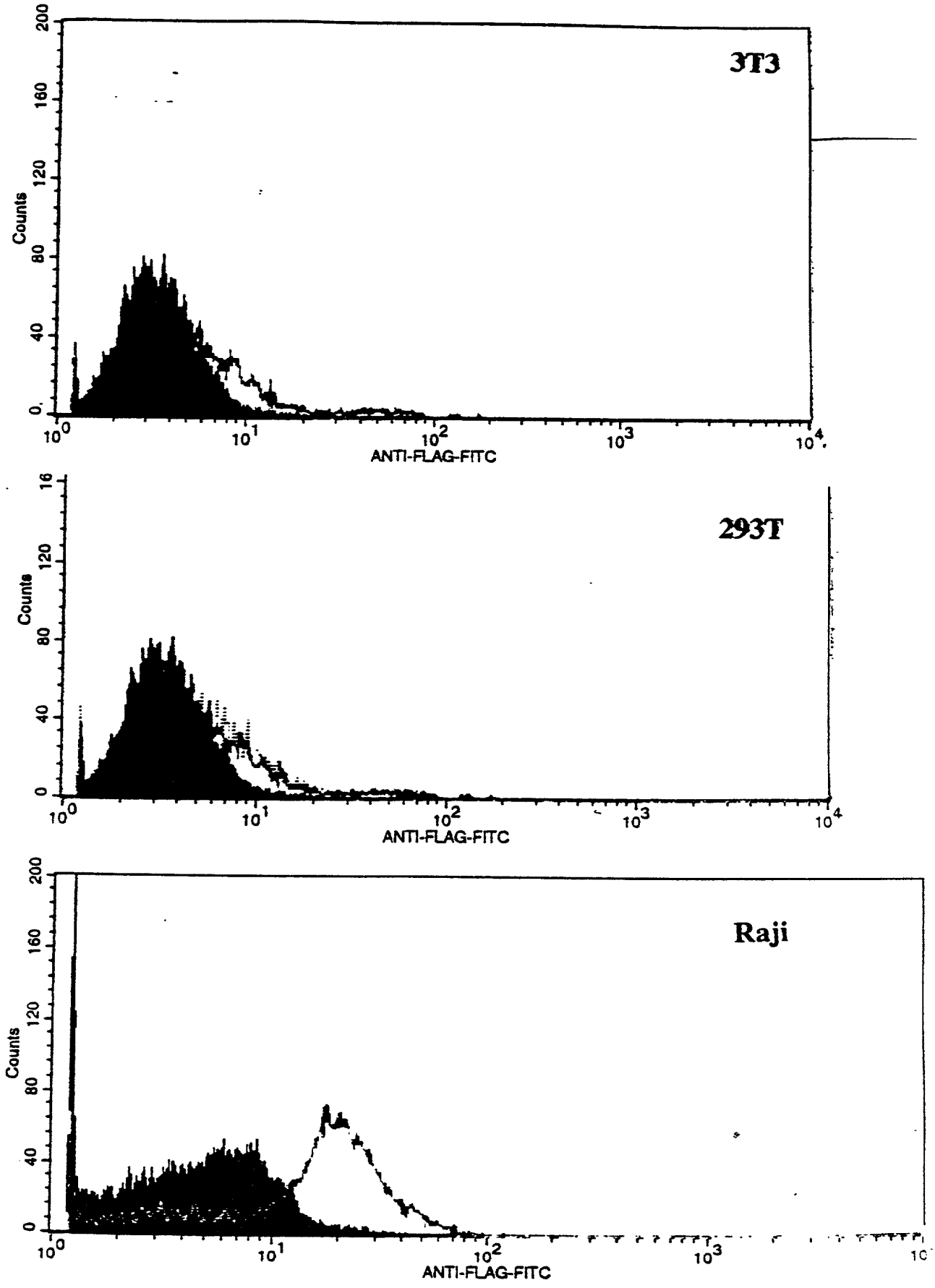


FIGURE 5B


3T3
293T
Raji
Counts
ANTI-FLAG-FITC
0
40
80
120
160
200
10^0
10^1
10^2
10^3
10^4

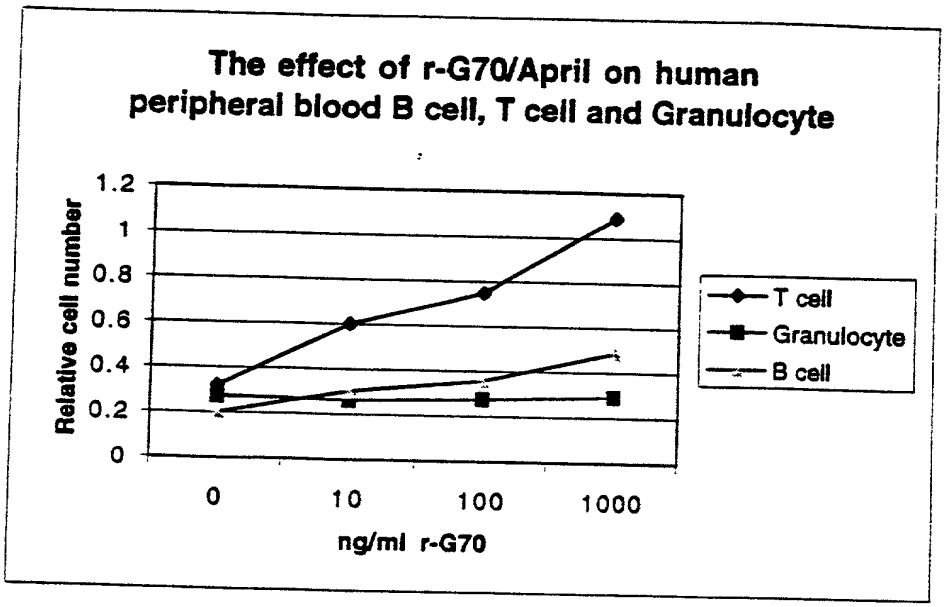
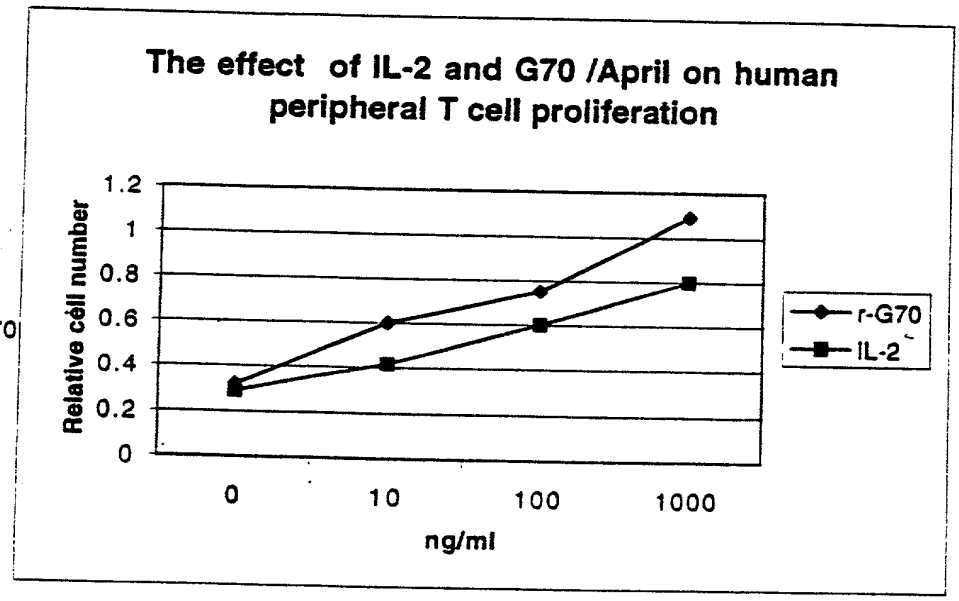

The effect of r-G70/April on human peripheral blood B cell, T cell and Granulocyte
Relative cell number
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml r-G70
T cell
Granulocyte
B cell

Fig. 6


The effect of IL-2 and G70 /April on human peripheral T cell proliferation
Relative cell number
1.2
1
0.8
0.6
0.4
0.2
0
0
10
100
1000
ng/ml
r-G70
IL-2

r-G70

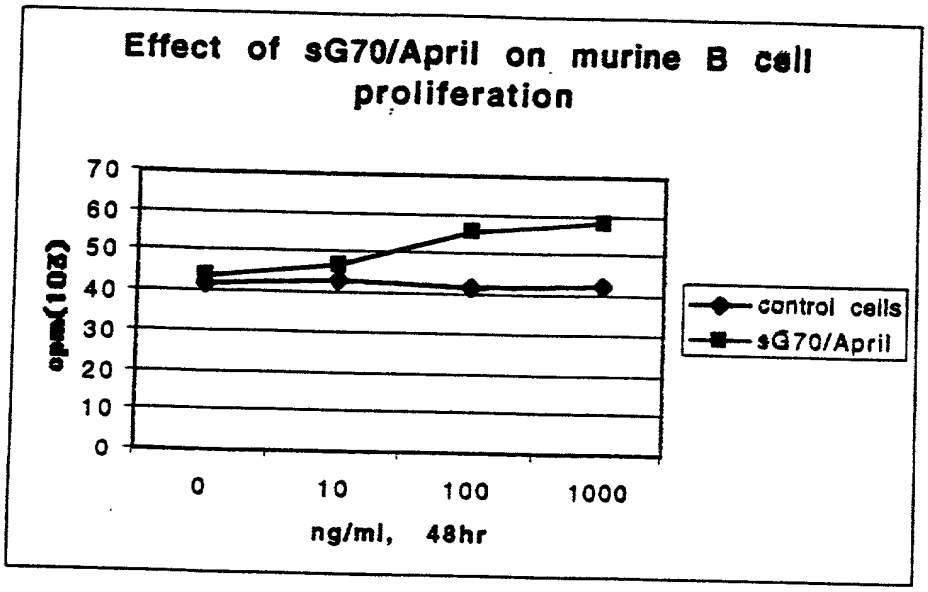

Effect of sG70/April on murine B cell proliferation
70
60
50
40
30
20
10
0
cpm(10Z)
0
10
100
1000
ng/ml, 48hr
control cells
sG70/April

Fig. 7

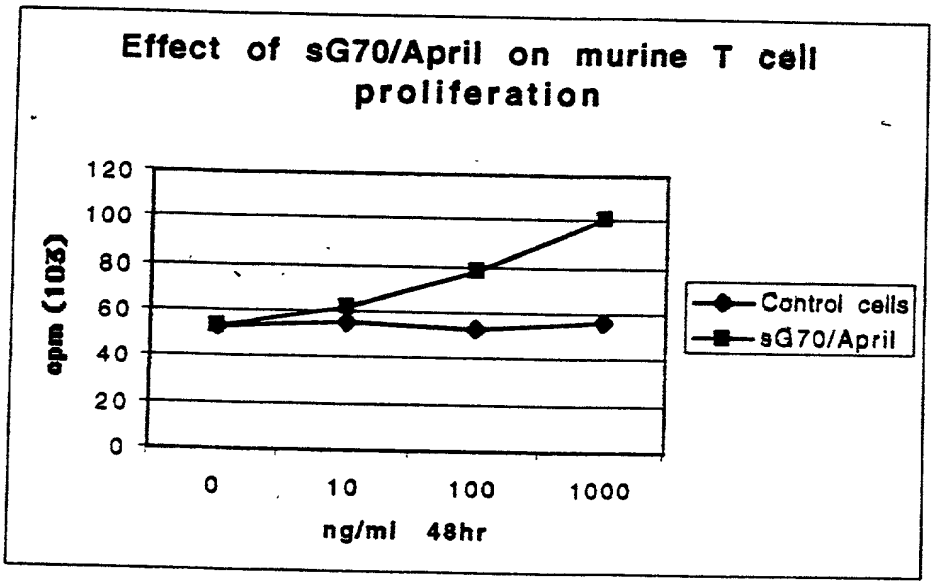

Effect of sG70/April on murine T cell proliferation
120
100
80
60
40
20
0
cpm (10Z)
0
10
100
1000
ng/ml 48hr
Control cells
sG70/April

Fig. 8

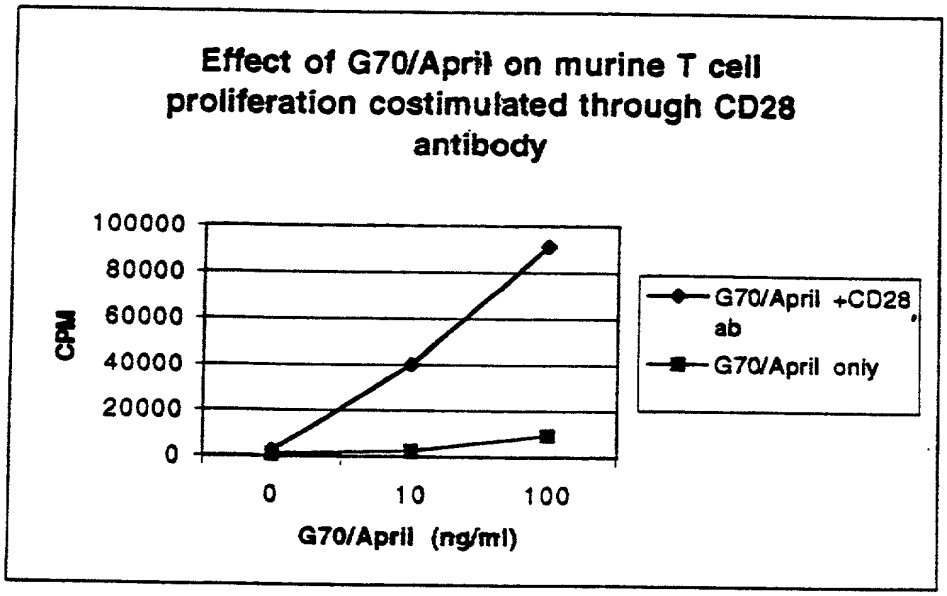

Effect of G70/April on murine T cell proliferation costimulated through CD28 antibody
CPM
100000
80000
60000
40000
20000
0
0
10
100
G70/April (ng/ml)
G70/April +CD28 ab
G70/April only

Fig. 9

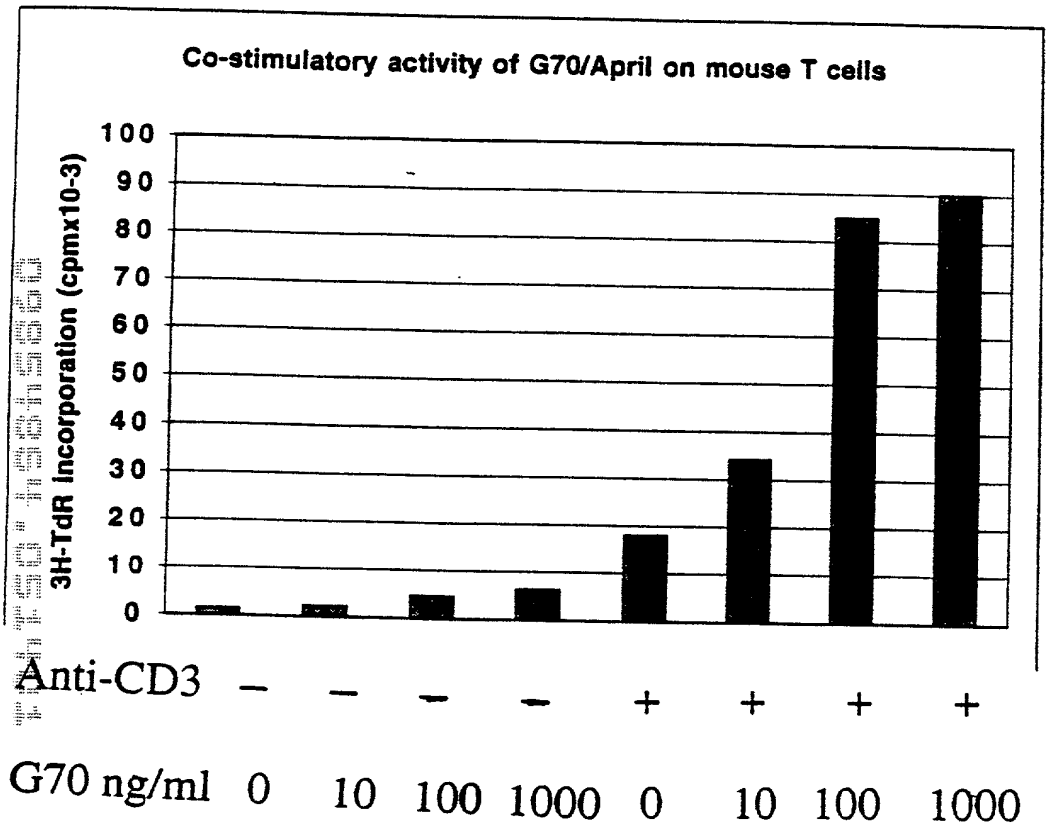

Co-stimulatory activity of G70/April on mouse T cells
3H-TdR incorporation (cpmx10-3)
100
90
80
70
60
50
40
30
20
10
0
Anti-CD3 – – – – + + + +
G70 ng/ml 0 10 100 1000 0 10 100 1000

Figure 10A

Human BCMA

Human (SEQ ID NO: 5):

1 MAGQCSQNEY FDSLLHACIP CQLRCSSNTP PLTCQRYCNA SVTNSVKGTN

51 AILWTCLGLS LIISLAVFVL MFLLRKISSE PLKDEFKNTG SGLLGMANID

101 LEKSRTGDEI ILPRGLEYTV EECTCEDCIK SKPKVDSDHC FPLPAMEEGA

151 TILVTTKTND YCKSLPAALS ATEIEKSISA R

Human (SEQ ID NO: 5):

MAGQ**CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY** CNASVTNSVK

GTNA ILWTCL GLSLIISLAV FVLMFLLRKI SSEPLKDEFK NTGSGLLGMA

NIDLEKSRTG DEIILPRGLE YTVEECTCED CIKSKPKVDS DHCFPLPAME

EGATILVTTK TNDYCKSLPA ALSATEIEKS ISAR

hBCMA's extracellular domain (SEQ ID NO: 6):

MAGQCSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY CNASVTNSVK

GTNA

hBCMA's cysteine-rich consensus region (SEQ ID NO: 7):

CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C

hBCMA's transmembrane region (SEQ ID NO: 8):

ILWTCL GLSLIISLAV FVLMF

Figure 10B

huBCMA-Fc (SEQ ID NO: 9):

MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNA
GGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK*

muBCMA-Fc (SEQ ID NO: 10):

MAQQCFHSEYFDSLLHACKPCHLRCSNPPATCQPYCDPSVTSSVKGSYTG
GGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK*

Figure 11
Alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence

murine BCMA amino acid sequence Length: 185 (SEQ ID NO: 11):

```
  1  MAQQCFHSEY FDSLLHACKP CHLRCSNPPA TCQPYCDPSV TSSVKGTYTV
 51  LWIFLGLTLV LSLALFTISF LLRKMNPEAL KDEPQSPGQL DGSAQLDKAD
101  TELTRIRAGD DRIFPRSLEY TVEECTCEDC VKSKPKGDSD HFFPLPAMEE
151  GATILVTTKT GDYGKSSVPT ALQSVMGMEK PTHTR
```

alignment of human BCMA amino acid sequence and murine BCMA amino acid sequence.

```
Query:     4 MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNAILWTCLGLS 63
             MA QC  +EYFDSLLHAC PC LRCS+  PP TCQ YC+ SVT+SVKGT  +LW  LGL+
Sbjct:     1 MAQQCFHSEYFDSLLHACKPCHLRCSN--PPATCQPYCDPSVTSSVKGTYTVLWIFLGLT 58

Query:    64 LIISLAVFVLMFLLRKISSEPLKDEFKNTG----SGLLGMANIDLEKSRTGDEIILPRGL 119
             L++SLA+F + FLLRK++ E LKDE ++ G    S  L  A+ +L + R GD+ I PR L
Sbjct:    59 LVLSLALFTISFLLRKMNPEALKDEPQSPGQLDGSAQLDKADTELTRIRAGDDRIFPRSL 118

Query:   120 EYTVEECTCEDCIKSKPKVDSDHCFPLPAMEEGATILVTTKTNDYCKS-LPAAL-SATEI 177
             EYTVEECTCEDC+KSKPK DSDH FPLPAMEEGATILVTTKT DY KS +P AL S   +
Sbjct:   119 EYTVEECTCEDCVKSKPKGDSDHFFPLPAMEEGATILVTTKTGDYGKSSVPTALQSVMGM 178

Query:   178 EKSISAR 184
             EK    R
Sbjct:   179 EKPTHTR 185
```

Figure 12A

Human TACI

huTACI (SEQ ID NO: 14).

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYSTLGLC LCAVLCCFLV AVACFLKKRG DPCSCQPRSR

201 PRQSPAKSSQ DHAMEAGSPV STSPEPVETC SFCFPECRAP TQESAVTPGT

251 PDPTCAGRWG CHTRTTVLQP CPHIPDSGLG IVCVPAQEGG PGA

MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCMSC
KTICNHQSQRTCAAFCRSLSCRKEQGKFYDHLLRDCISCASICGQHPKQC
AYFCENKLRSPVNLPPELRRQRSGEVENNSDNSGRYQGLEHRGSEASPAL
PGLKLSADQVALVYSTLGLCLCAVLCCFLVAVACFLKKRGDPCSCQPRSR
PRQSPAKSSQDHAMEAGSPVSTSPEPVETCSFCFPECRAPTQESAVTPGT
PDPTCAGRWGCHTRTTVLQPCPHIPDSGLGIVCVPAQEGGPGA

huTACI's extracellular domain (SEQ ID NO: 15):

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

151 PGLKLSADQV ALVYST

Figure 12B

huTACI's cysteine-rich consensus region (SEQ ID NO: 16):
CPEEQYWDPLLGTCMSCKTICNHQSQRTCAAFC and
CRKEQGKFYDHLLRDCISCASICGQHPKQCAYFC

transmembrane region (SEQ ID NO: 17):
LGLCLCAVLCCFLVAVACFL

hTACI-Fc (SEQ ID NO: 18):

```
1   MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCMSC

      51   KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC

     101   AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL

     151   PGLKLSADQV ALVYSGGGGG DKTHTCPPCP APELLGGPSV FLFPPKPKDT

     201   LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY

     251   RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT

     301   LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTPPVLDS

     351   DGSFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK*
```

Figure 13

Alignment of cysteine rich extracellular regions of human TACI and human BCMA.

```
34 CPEEQYWDPLLGTCMSCKTICNHQS.QRTCAAFCRSLSCRKEQGKFYDHL 82
   | : :|.| ||  |. |.  |.  .   ||  :| .      .|   . :
 8 CSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGT..NAI 55

       83 LRDCISCASI 92
          |  |:  . |
       56 LWTCLGLSLI 65
```

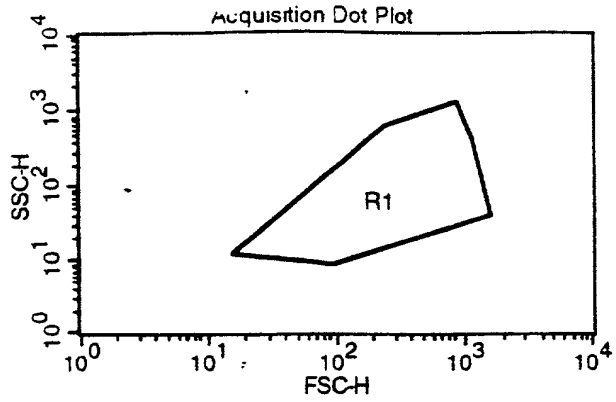
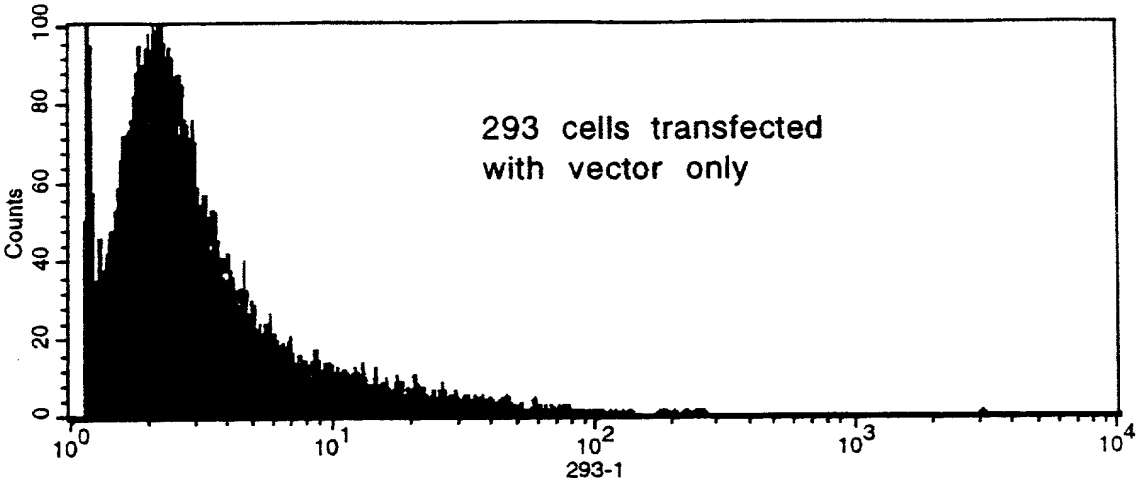
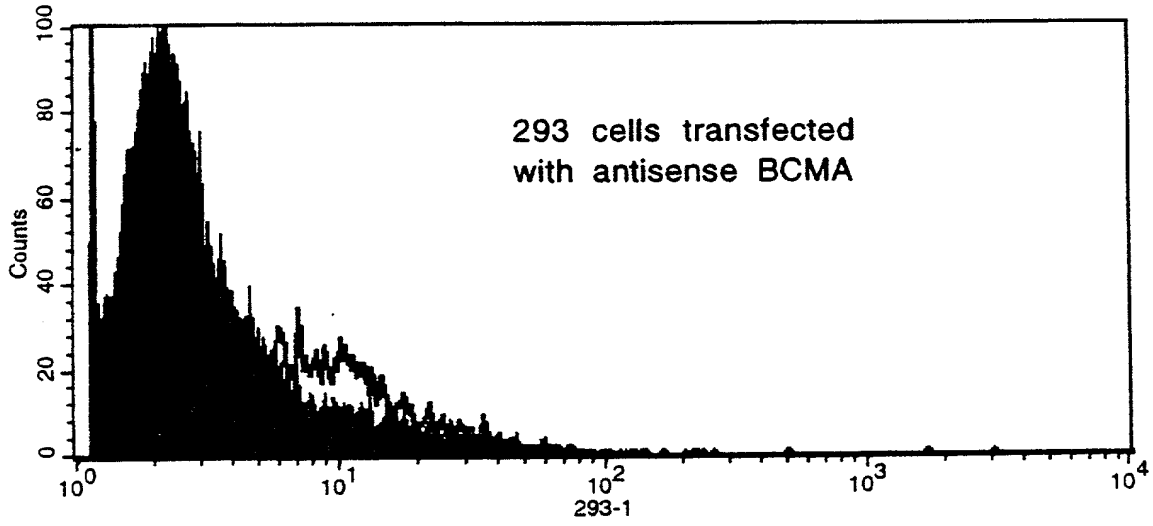


Fig.14



A.



B.

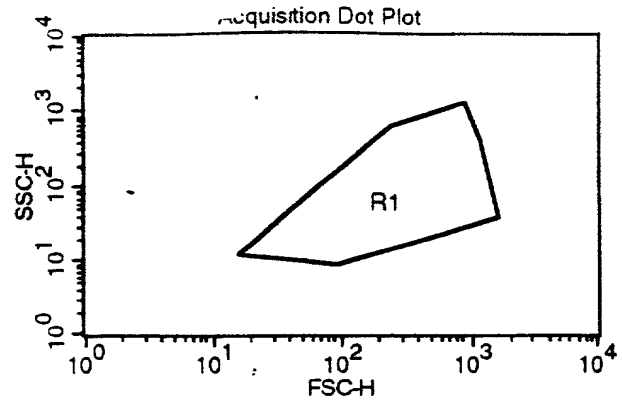
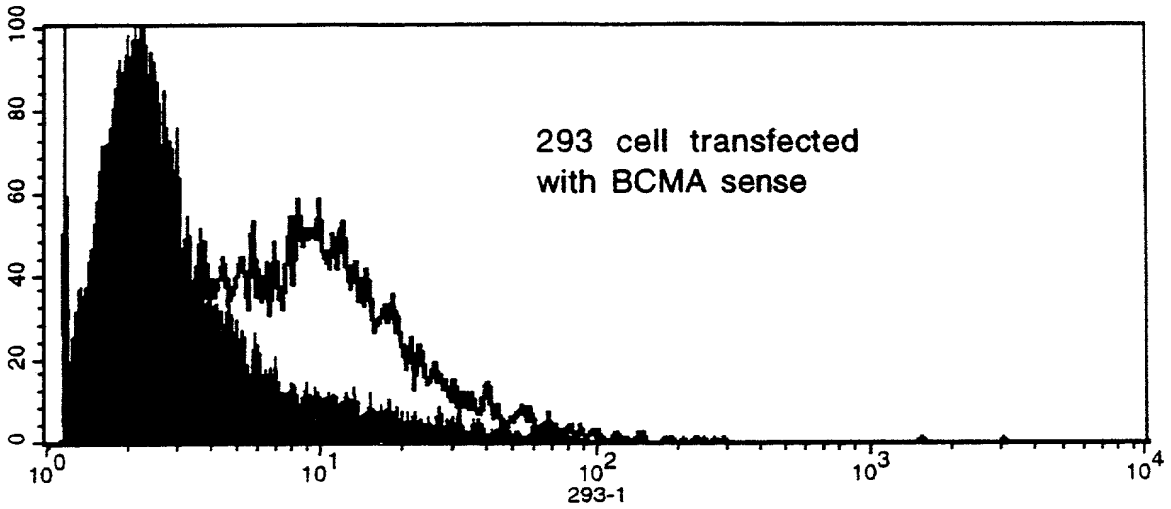

Acquisition Dot Plot
SSC-H
FSC-H
R1

Fig.14


293 cell transfected
with BCMA sense
Counts
293-1

C.

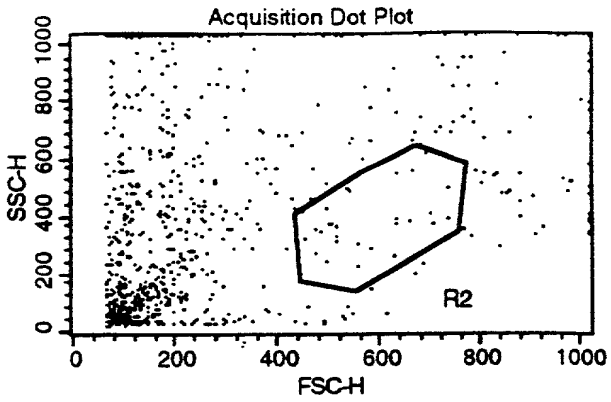
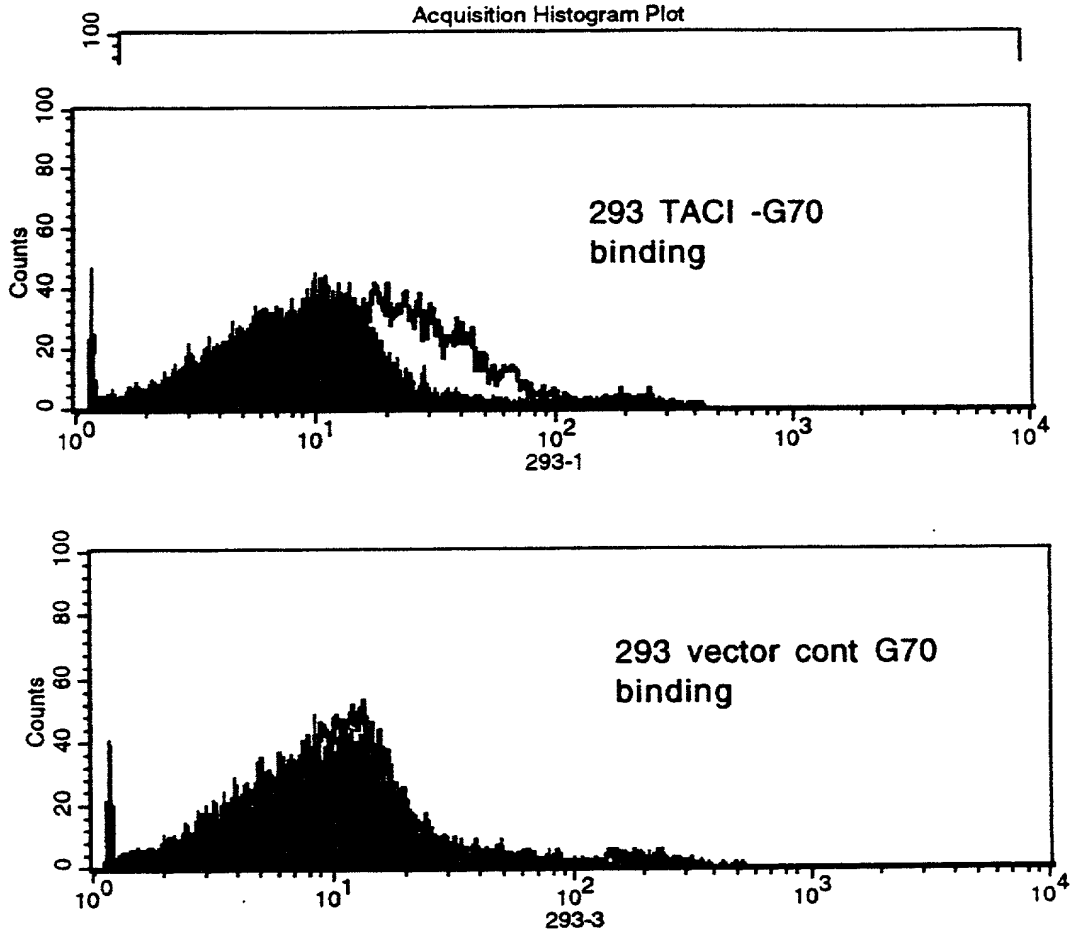

Acquisition Dot Plot
SSC-H
FSC-H
R2
0
200
400
600
800
1000

Fig. 15


Acquisition Histogram Plot
293 TACI -G70
binding
Counts
293-1
A.
293 vector cont G70
binding
Counts
293-3
B.

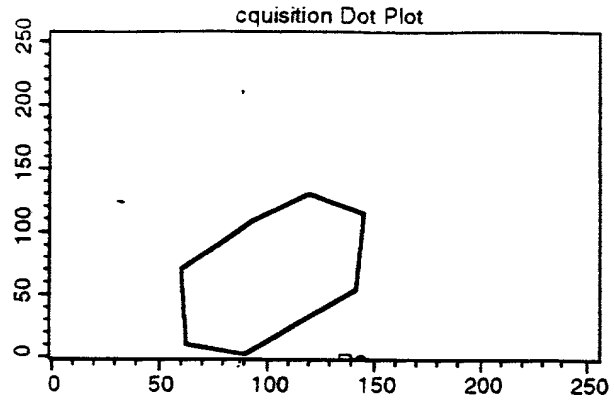
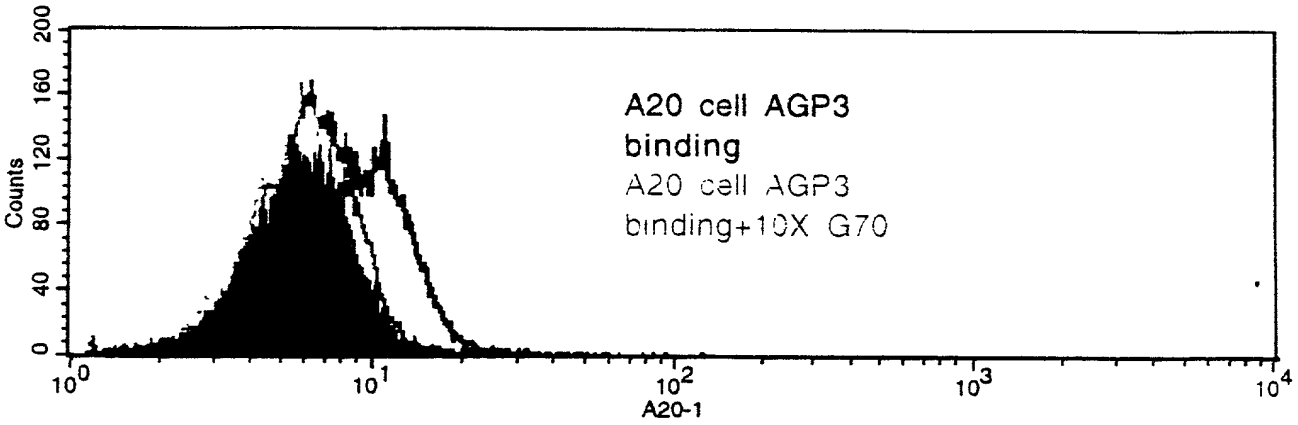
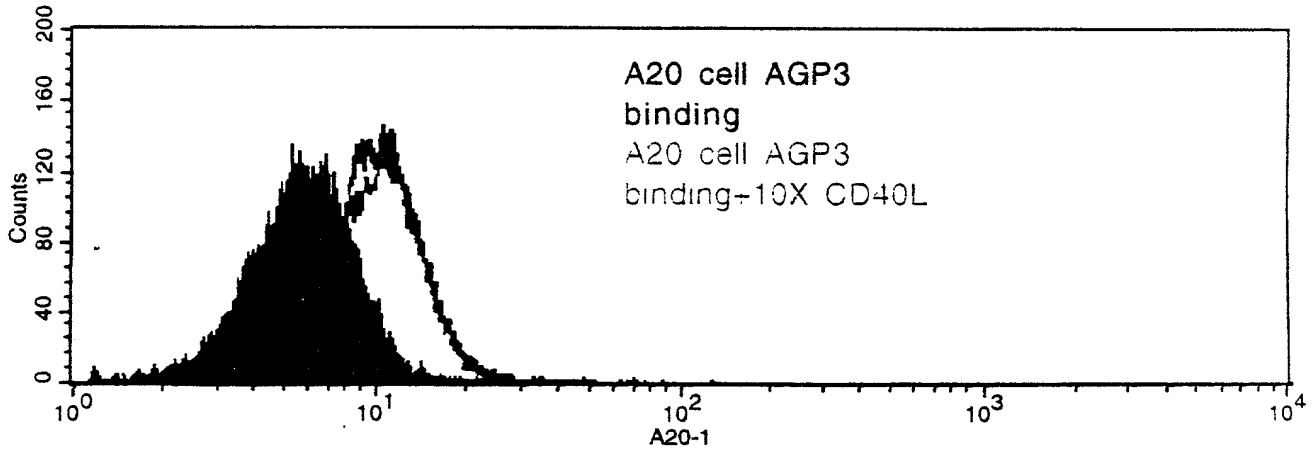


Fig. 16

A.



B.



Experiment 4-3-2000

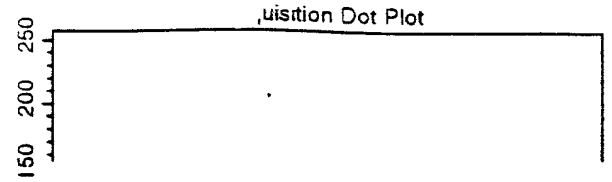
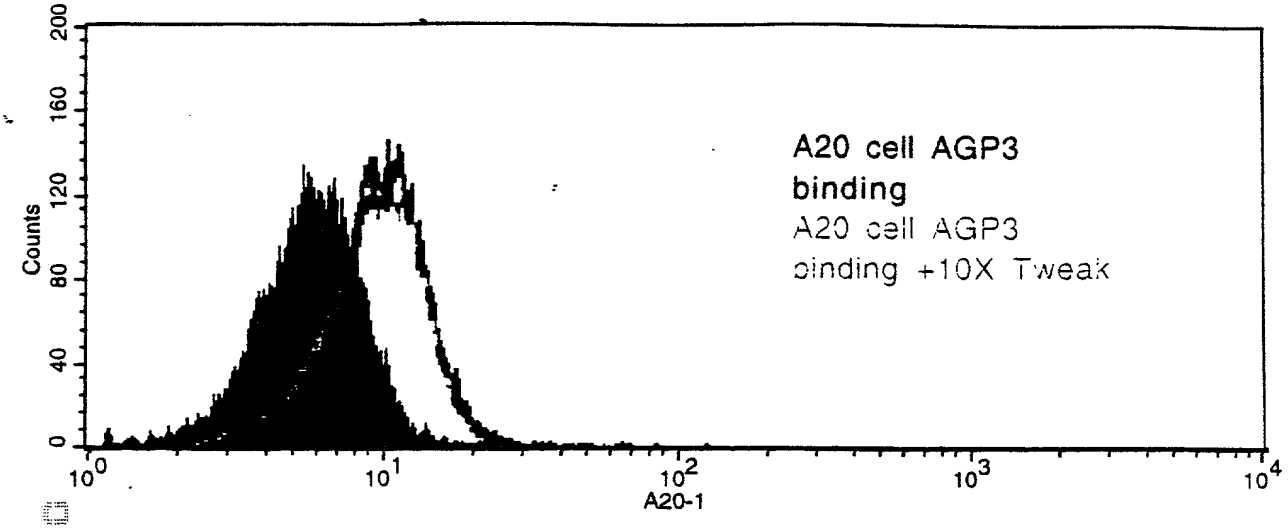
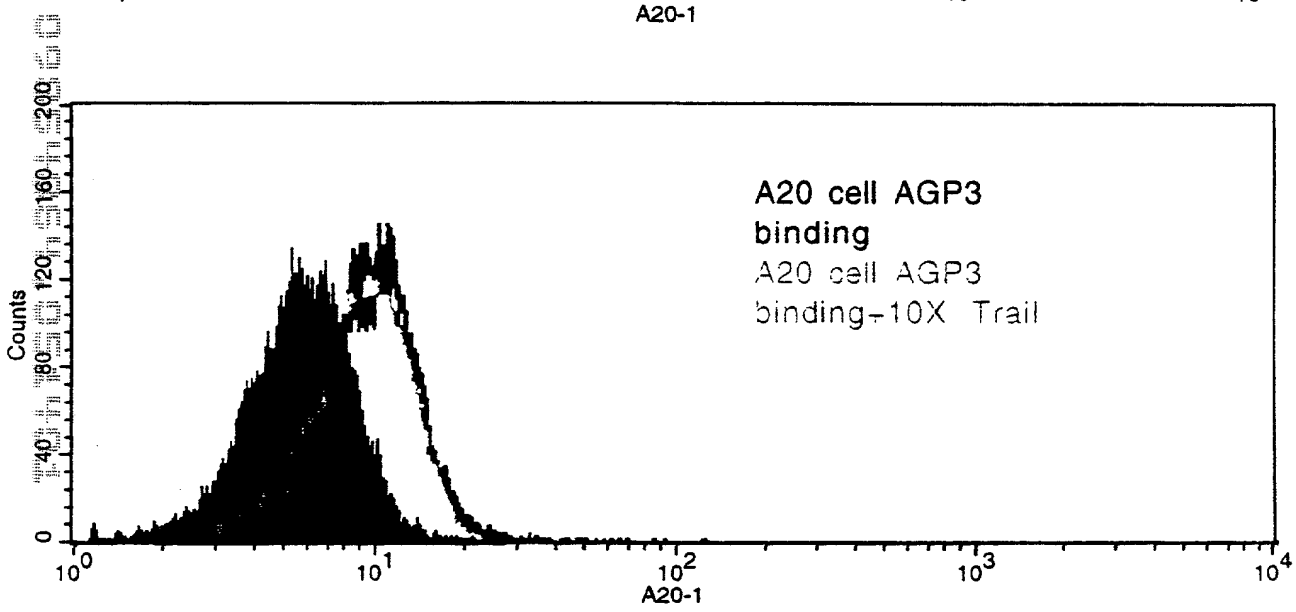


Fig. 16

C.

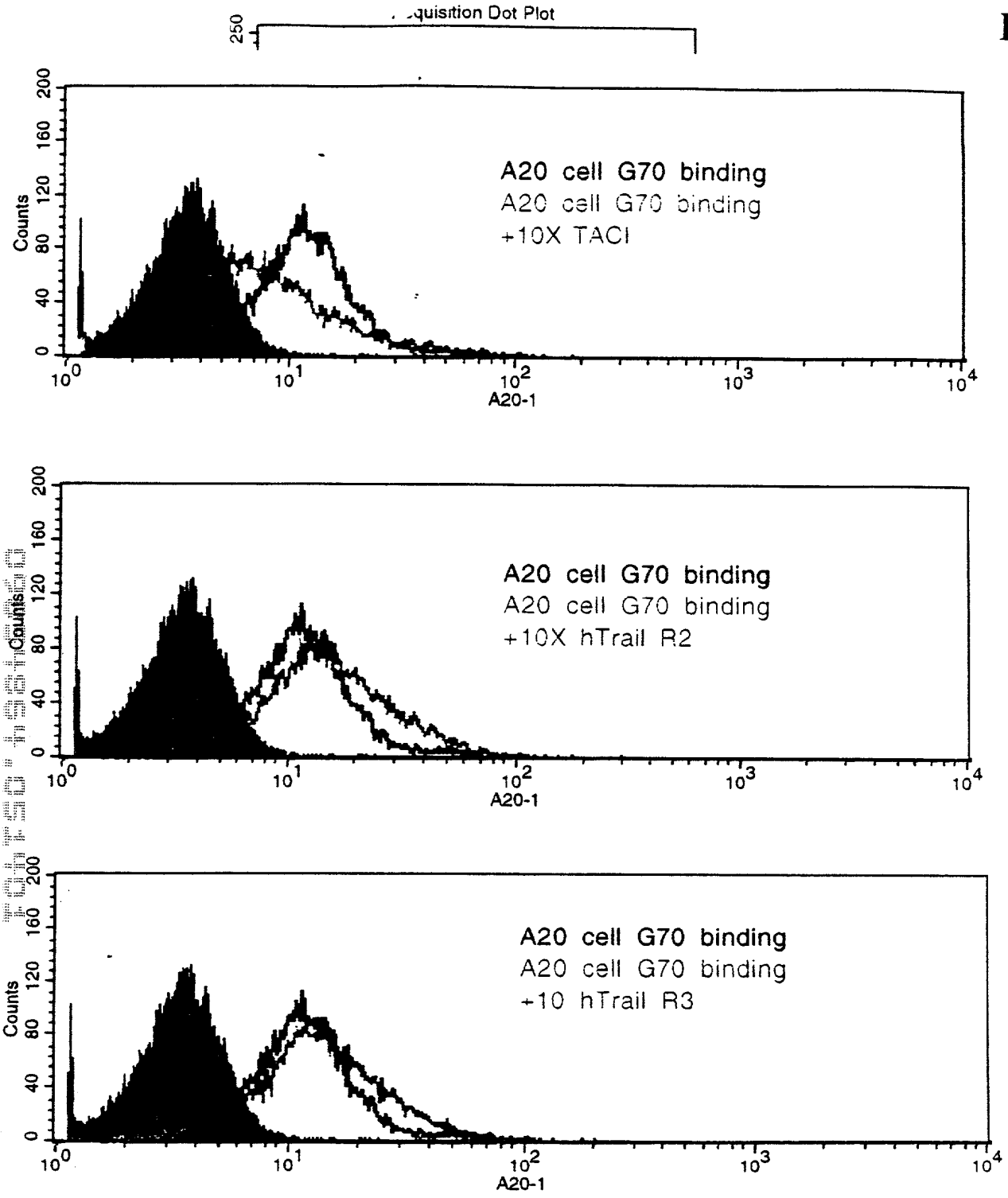


D.



Experiment 4-3-2000

Fig.17



Experiment
4-11-2000

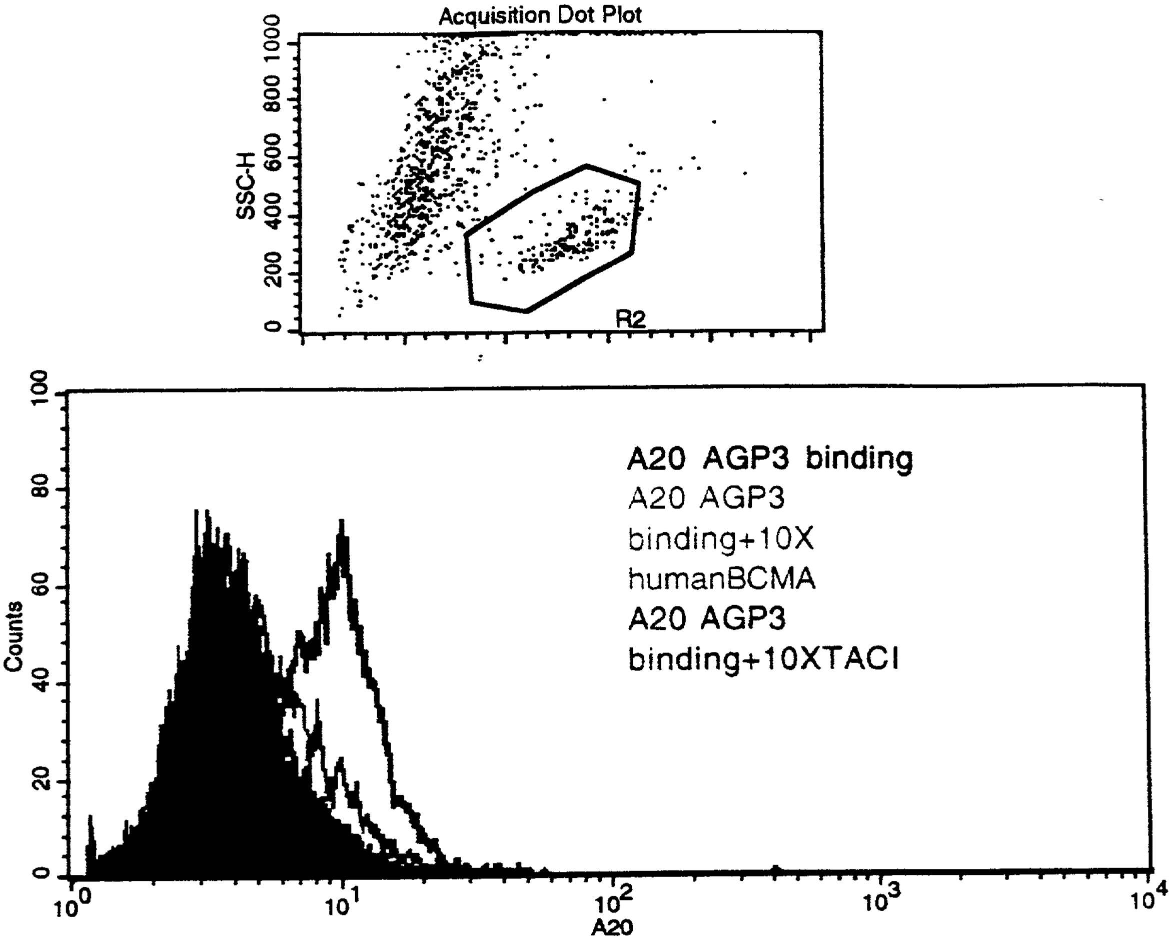

Acquisition Dot Plot
SSC-H
0
200
400
600
800
1000
R2
A20 AGP3 binding
A20 AGP3
binding+10X
humanBCMA
A20 AGP3
binding+10XTACI
Counts
0
20
40
60
80
100
10^0
10^1
10^2
10^3
10^4
A20

Fig.18

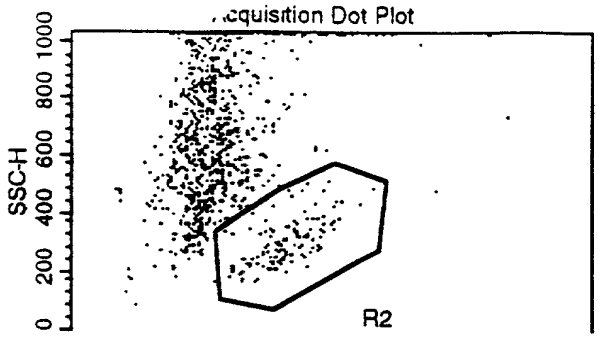
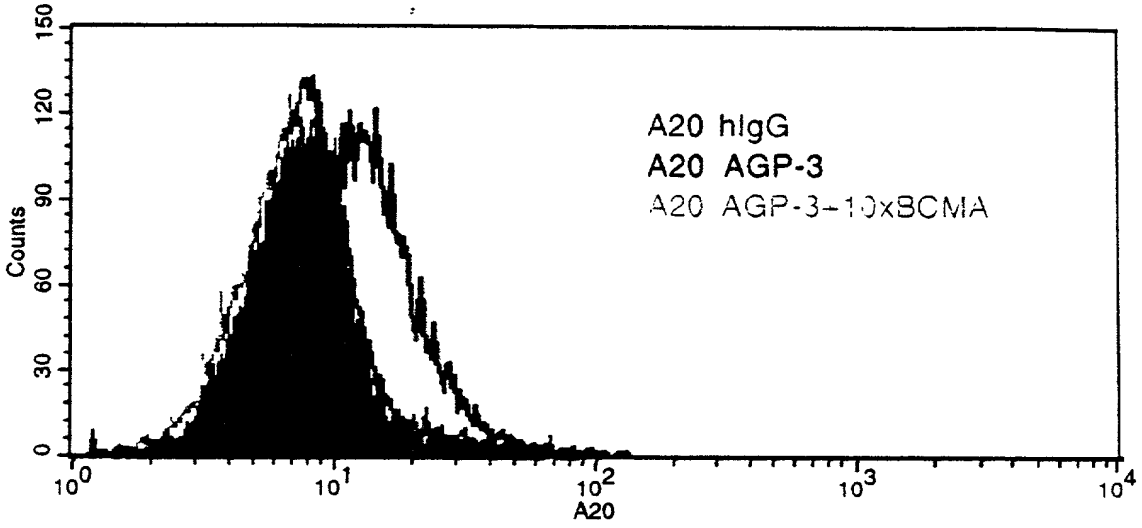

Acquisition Dot Plot
SSC-H
0
200
400
600
800
1000
R2

Fig.19


A.
A20 hIgG
A20 AGP-3
A20 AGP-3+10xBCMA
Counts
0
30
60
90
120
150
10^0
10^1
10^2
10^3
10^4
A20

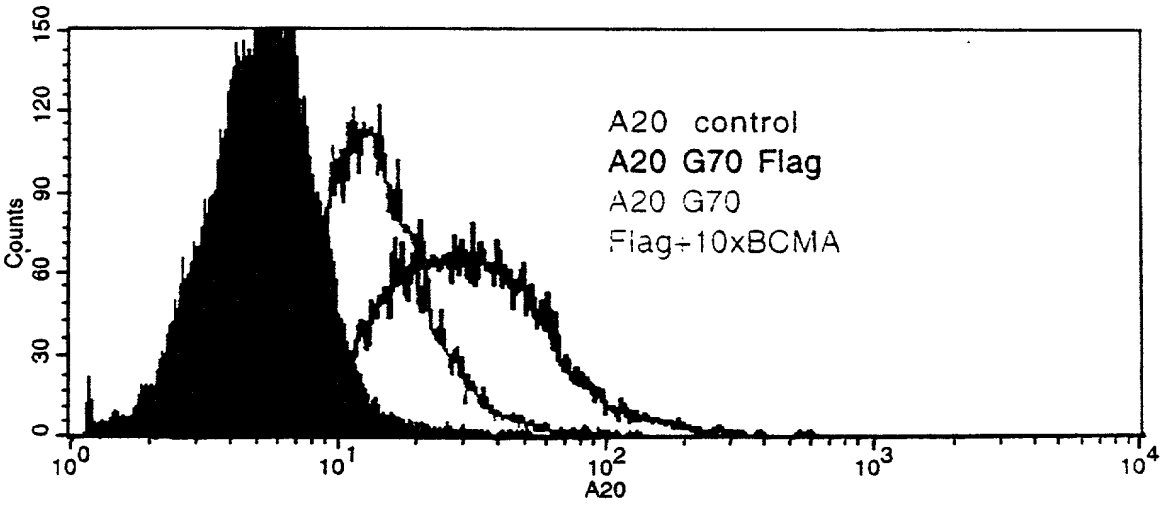

B.
A20 control
A20 G70 Flag
A20 G70
Flag+10xBCMA
Counts
0
30
60
90
120
150
10^0
10^1
10^2
10^3
10^4
A20

Fig.20

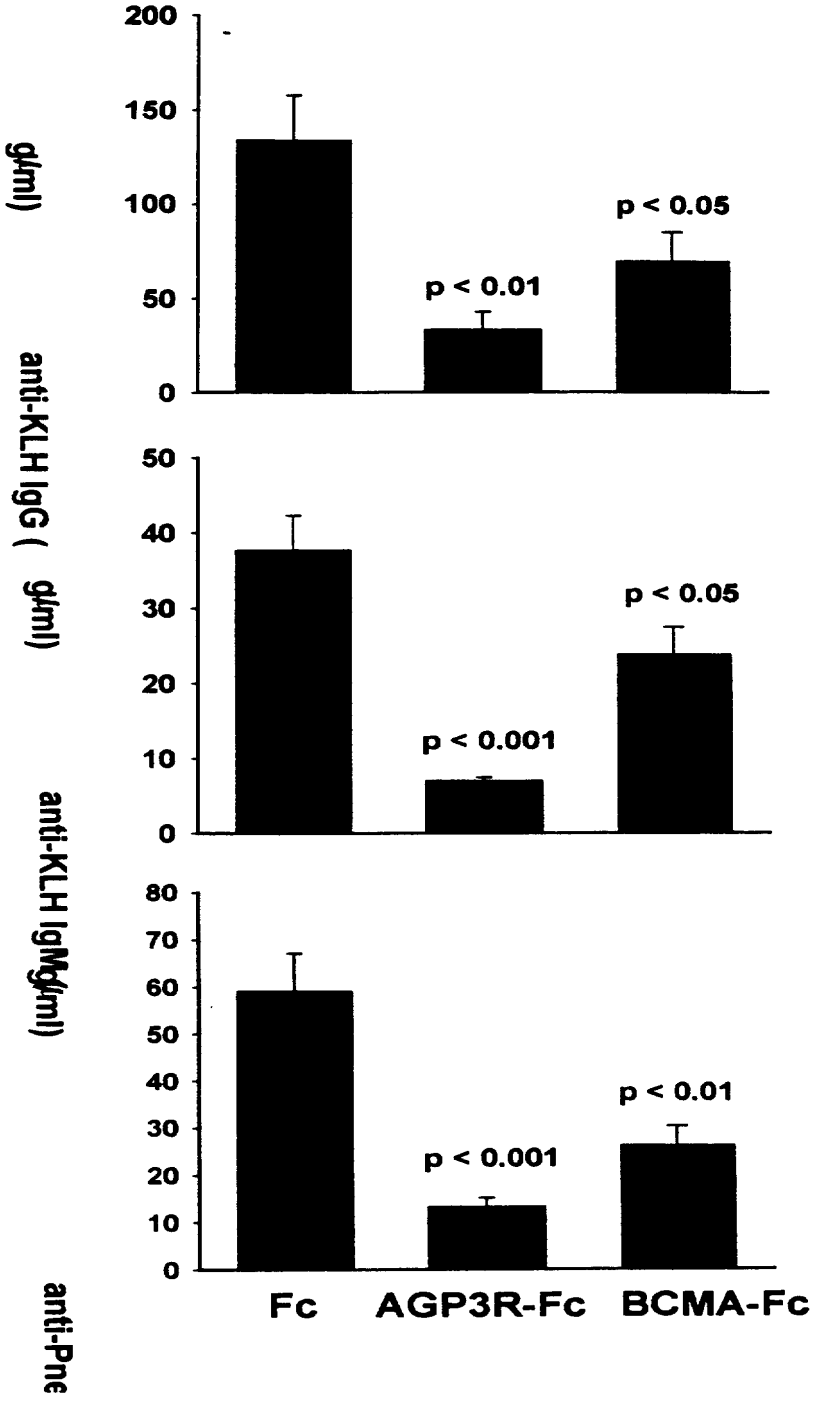


Figure 21 Fc-humanAPRIL

Fc-humanAPRIL protein sequence including the signal sequence, Fc domain, linker (XhoI site) and April:

```
   1 MEWSWVFLFF LSVTTGVHSD KTHTCPPCPA PELLGGPSVF
     LFPPKPKDTL
  51 MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP
     REEQYNSTYR
 101 VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG
     QPREPQVYTL
 151 PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY
     KTTPPVLDSD
 201 GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL
     SLSPGKSRAV
 251 LTQKQKKQHS VLHLVPINAT SKDDSDVTEV MWQPALRRGR
     GLQAQGYGVR
 301 IQDAGVYLLY SQVLFQDVTF TMGQVVSREG QGRQETLFRC
     IRSMPSHPDR
 351 AYNSCYSAGV FHLHQGDILS VIIPRARAKL NLSPHGTFLG
     FVKL*
```

Figure 22

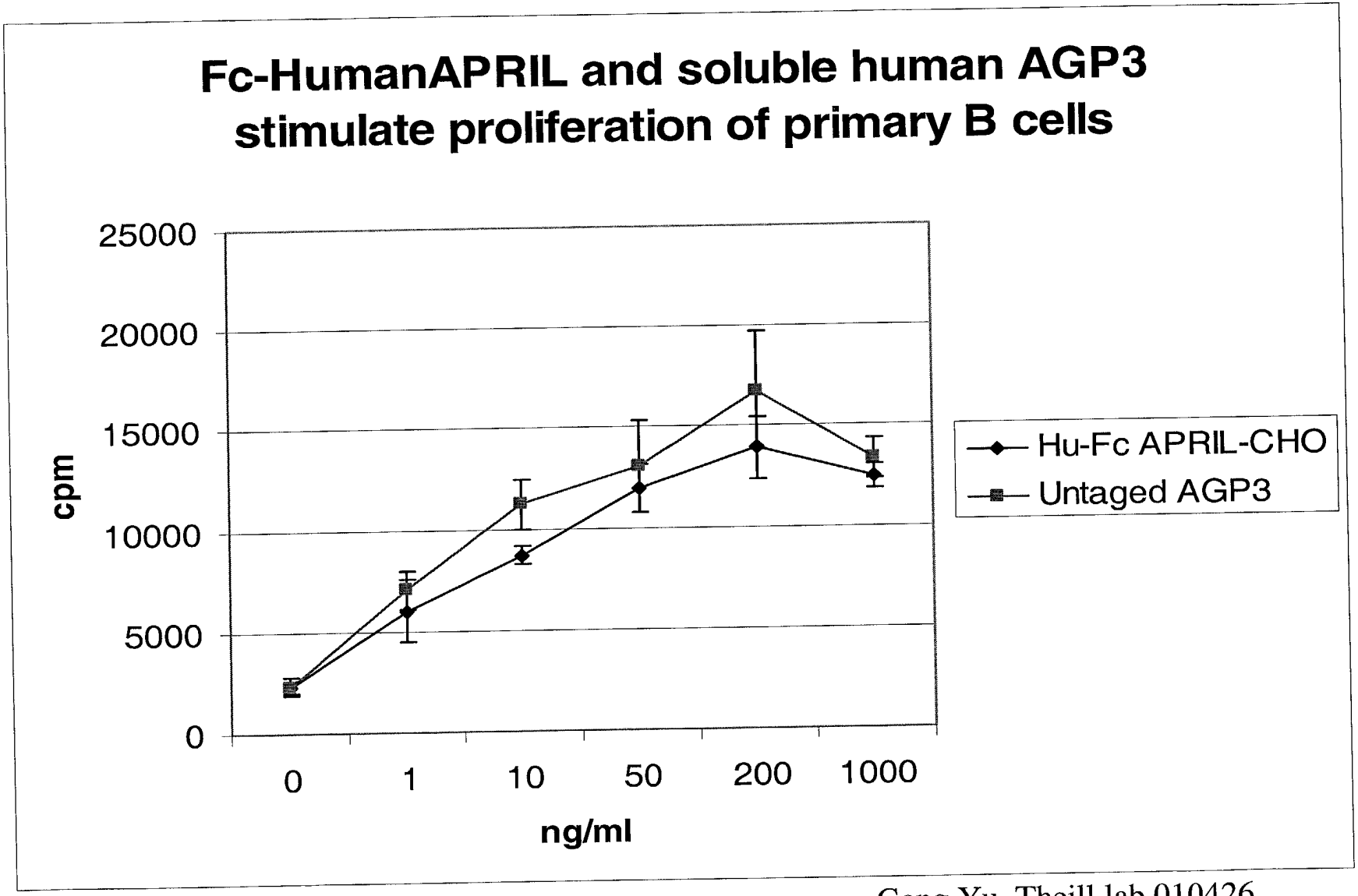


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Figure 23

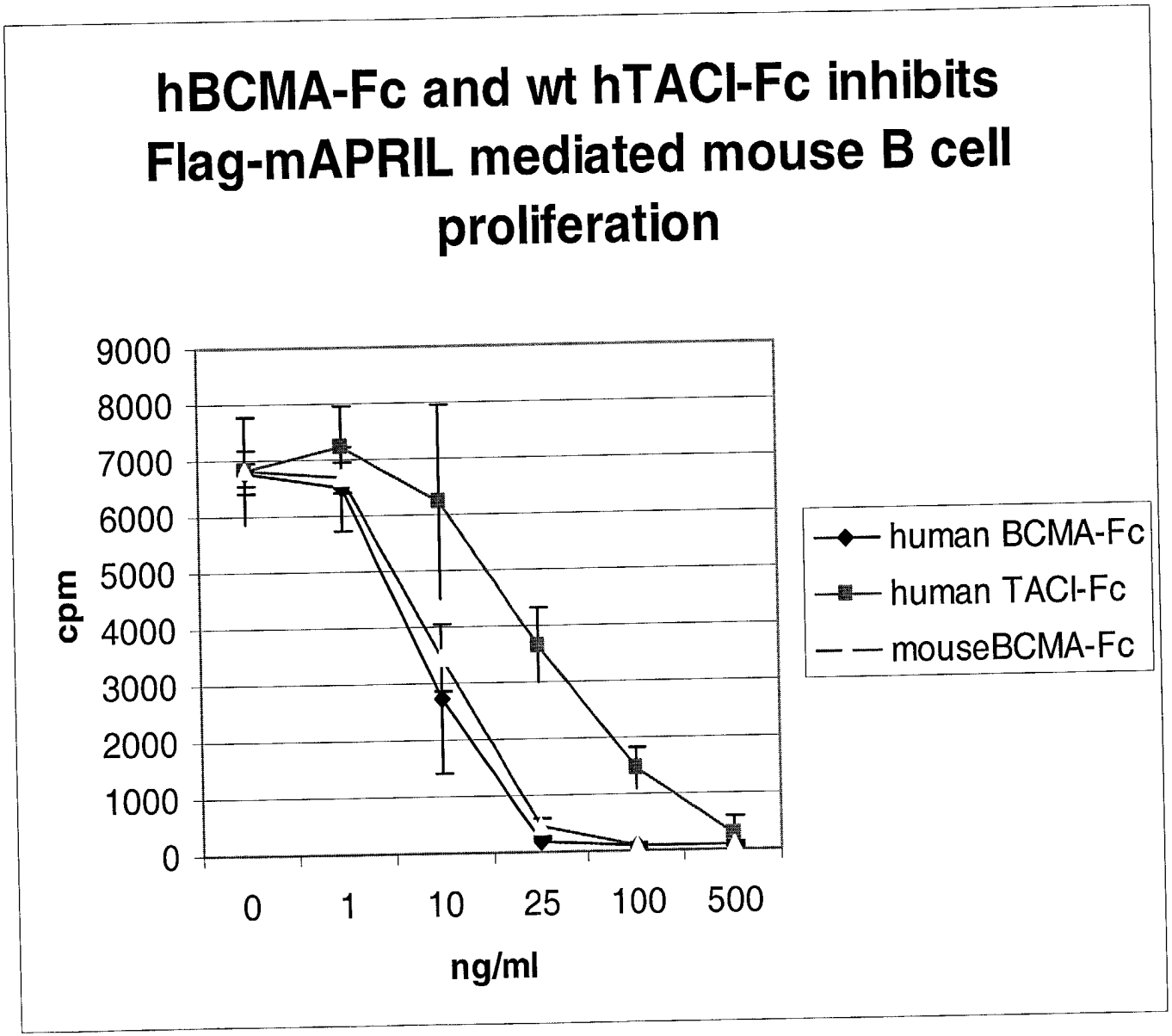

hBCMA-Fc and wt hTACI-Fc inhibits Flag-mAPRIL mediated mouse B cell proliferation
cpm
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0
1
10
25
100
500
ng/ml
human BCMA-Fc
human TACI-Fc
mouseBCMA-Fc

Figure 24:

hBCMA-Fc reduces PB B cell level *in vivo*

15 mg/kg ip on day 0, 3, and 6

BLOOD	WBC 10e6/ml	#Lym 10e6/ml	CD3+ #	CD3-B220+ #
BCMA-Fc	**5.30**	**3.81**	**2.3**	**1.3**
SD	0.39	0.43	0.32	0.27
t test	0.03318	0.01570	0.24737	0.00506
Fc	**8.02**	**6.43**	**2.7**	**3.2**
SD	1.27	1.52	0.6	0.6
Saline	**6.90**	**5.55**	**2.1**	**2.9**
SD	2.04	1.79	0.5	1.2

Figure 25

hBCMA-Fc reduces spleen B cell levels *in vivo*

15 mg/kg ip on day 0, 3, and 6

spleen	WBC 10e6/ml	Lym (%)	spleen lym# 10ml(x10e6)	CD3-B220+ (%)	CD3-B220+ #
BCMA-Fc	**9.12**	**97.9**	**89.3**	**45.5**	**41.8**
SD	0.92	0.51	9.32	1.29	4.92
t test	0.02778	0.89118	0.02668	0.00234	0.02088
Fc	**11.49**	**97.9**	**112.5**	**50.6**	**57.1**
SD	1.62	0.38	15.65	1.95	9.67
Saline	**11.48**	**98.5**	**113.1**	**53.7**	**48.5**
SD	1.71	0.1	16.9	6.7	29.15

Figure 26

Flag-mAPRIL and hAGP3 mediated IgA production inhibited by hBCMA-Fc and hTACI-Fc *in vitro*

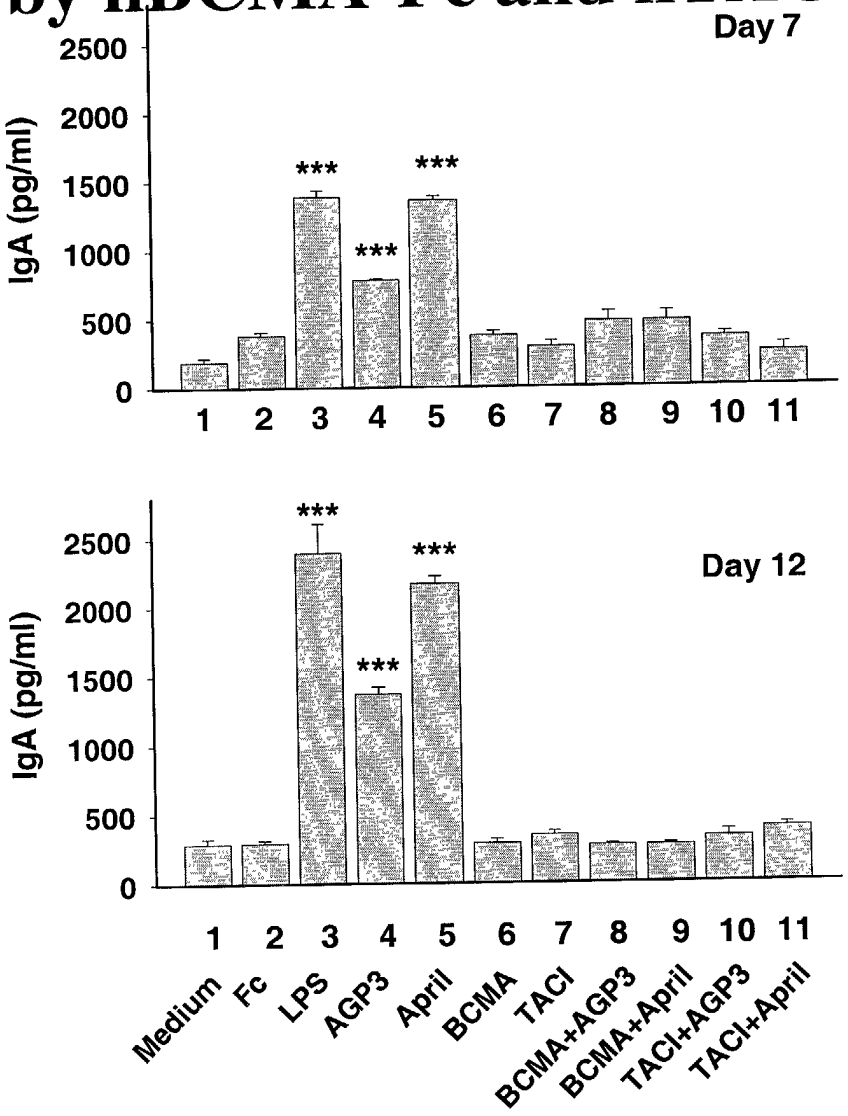


Figure 27

Flag-mAPRIL and hAGP3 Mediated IgG Production Inhibited by BCMA-Fc and TACI-Fc *in Vitro*

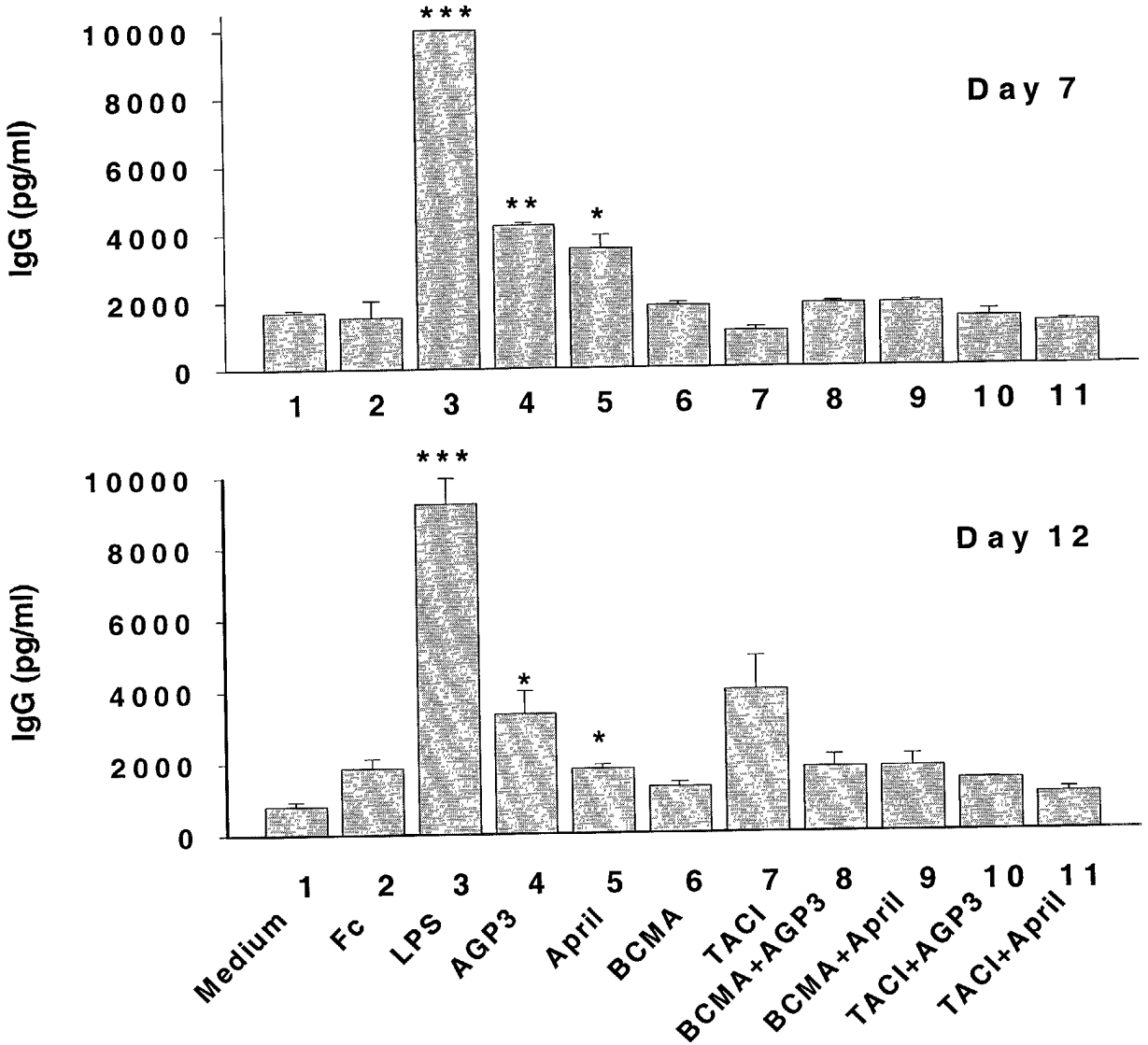


Figure 28: Significantly reduces total IgE and IgA in normal mice treated with mBCMA-Fc and trun hTACI-Fc

5 mg/kg ip day 0, 3, and 6

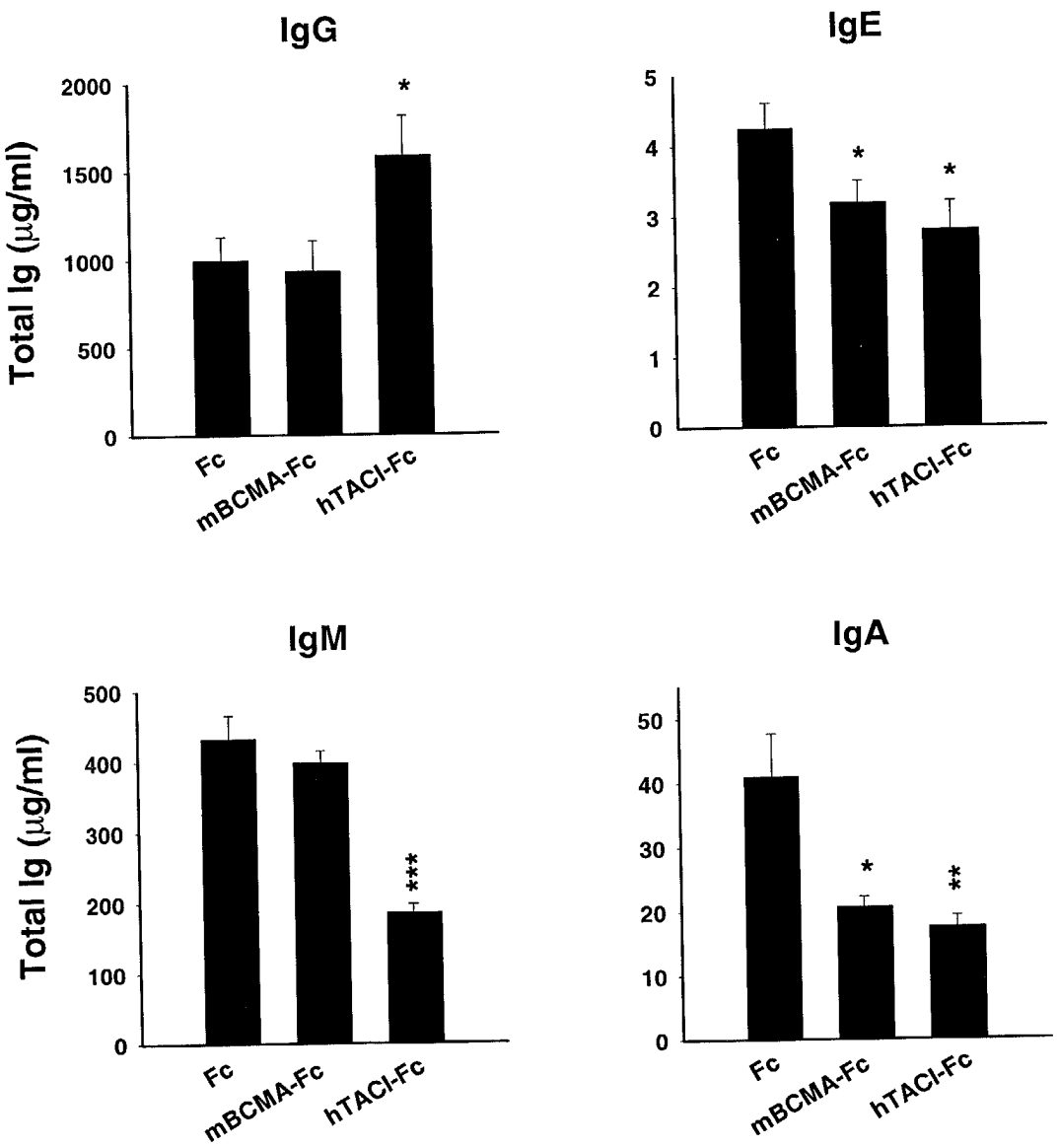


Figure 29: BCMA-Fc and truncated TACI-Fc at daily doses of 0.5 mg/kg inhibits humoral immunity *in vivo*

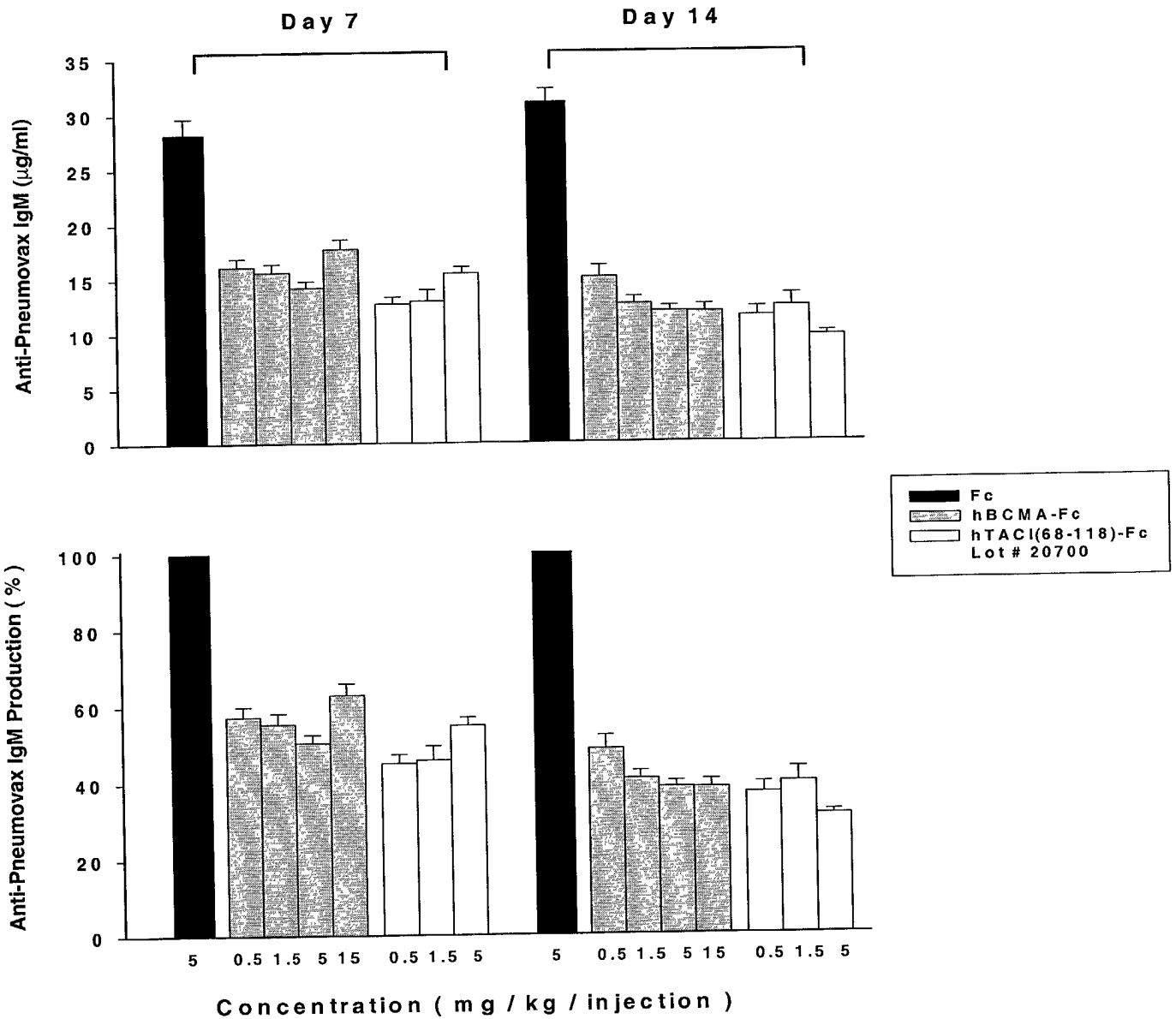


Figure 30: Anti-mAPRIL c-19 MAb inhibition of APRIL mediated B cell proliferation

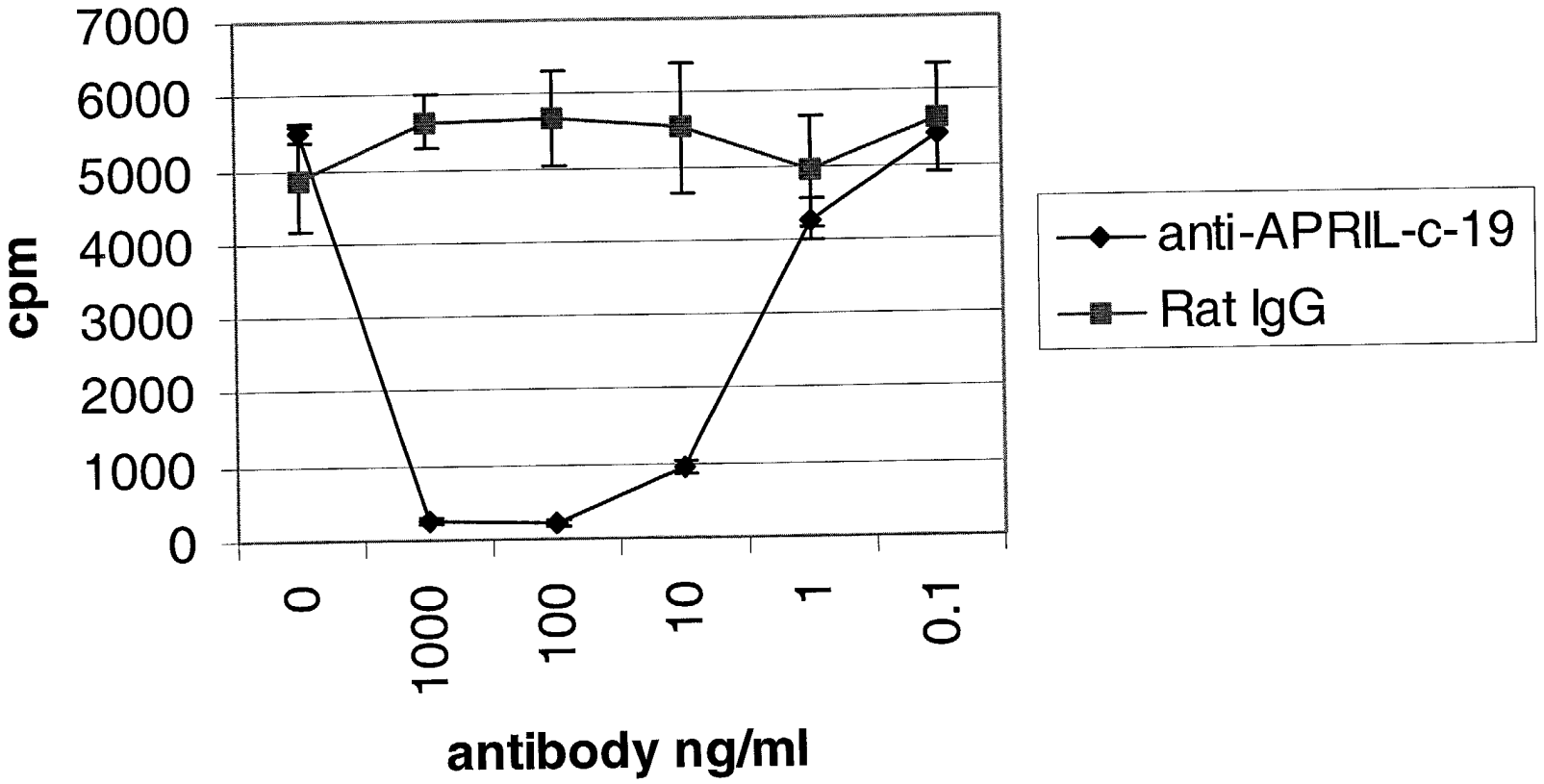
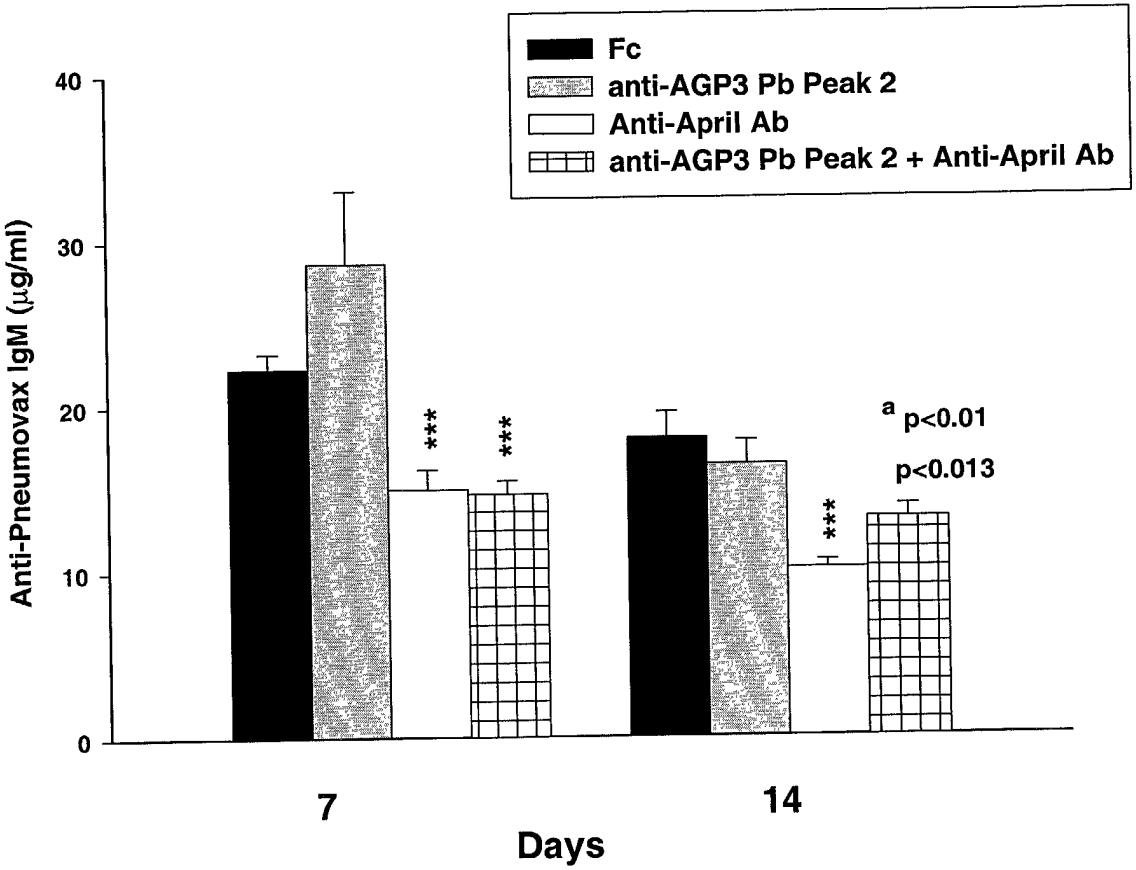


Figure 31

Neutralizing anti-mAPRIL Mab Reduces anti-Pheumovacs IgM *In Vivo*

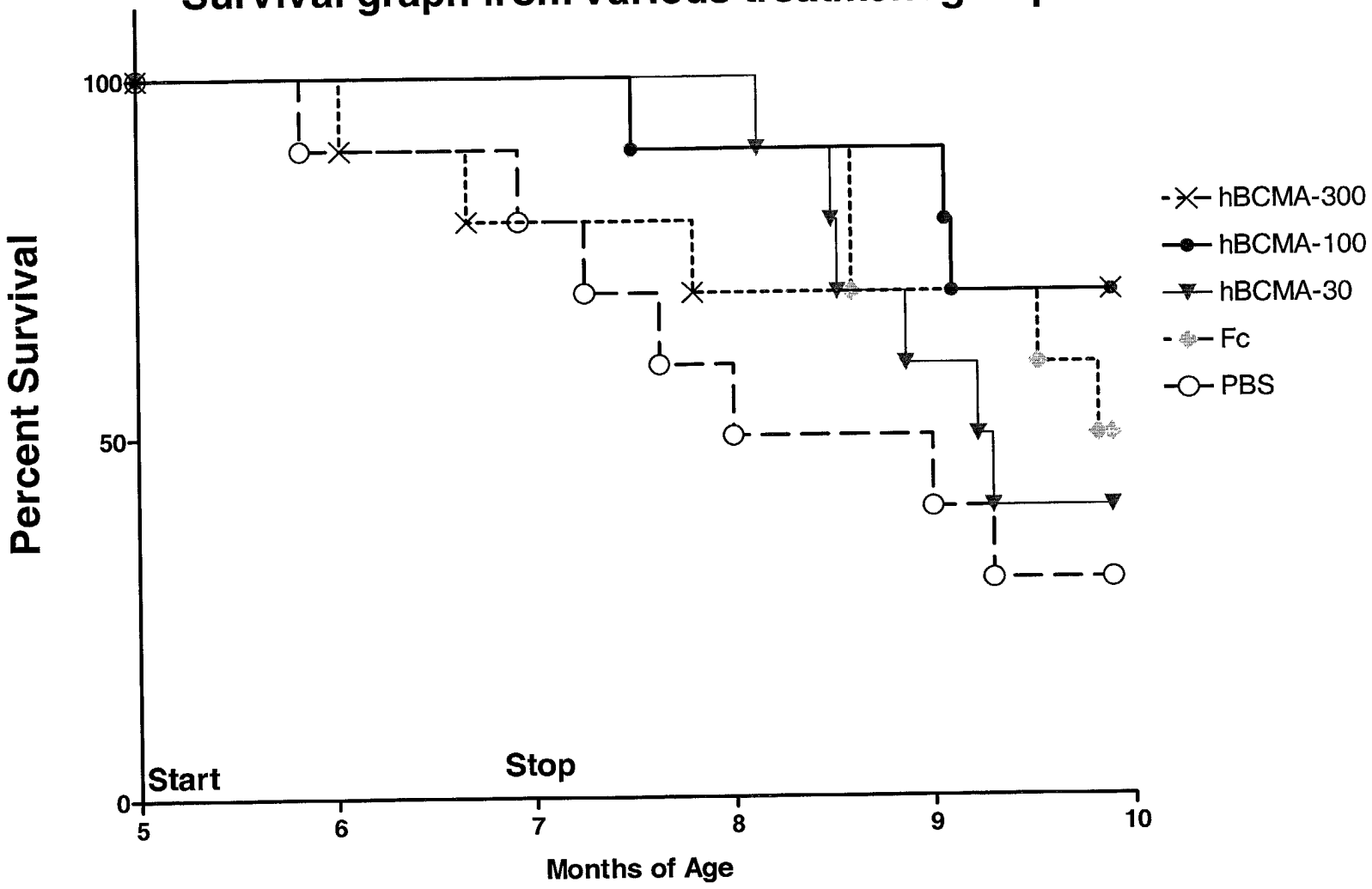
5 mg/kg ip on day 0, 3, and 6



[a] difference between Anti-April Ab and anti-AGP3 Pb Peak 2+ Anti-April Ab Groups

12.15.00 lupus exp.

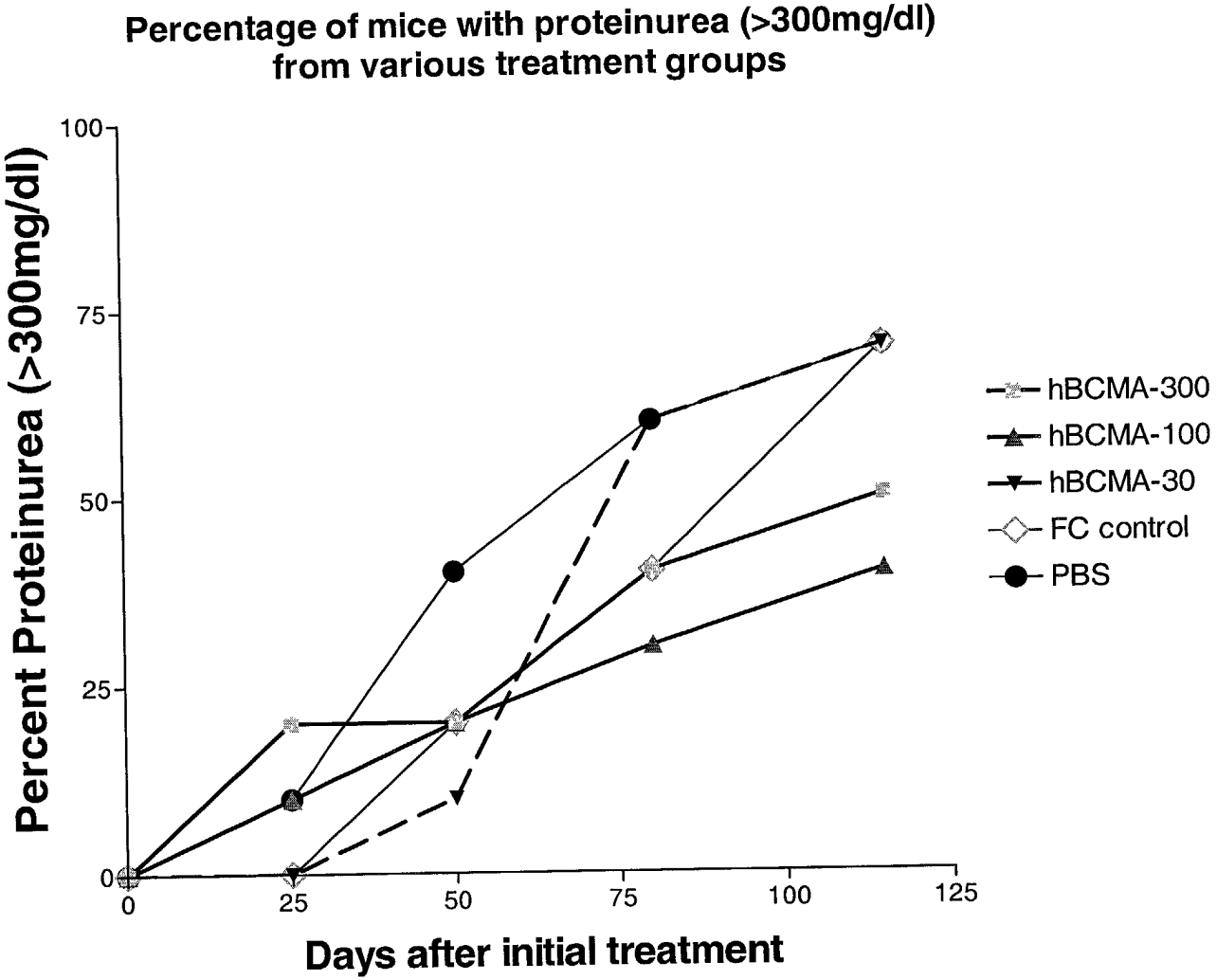
Figure 32: Effect of hBCMA-Fc in NCB/NCWF1 mice



N=10 Mice were treated for 8 weeks 3x/week with the indicated proteins. KIN2 group had 12 mice. The 100 in the legend stands for 100 µg of protein or 4mg/kg i.p.

12.15.00 lupus exp

Figure 33: Effect of hBCMA-Fc in NCB/NCWF1 mice



N=10 Five month old BWF1 mice were treated with protein for 8 weeks i.p.
The hBCMA-300 stands for hBCMA-fc 300µg/mouse (12mg/kg)

Figure 34: Analysis of antibodies to dsDNA from the peripheral blood from various treatment groups of BWF1 at day 0,30,60, and 90.

MEAN anti-dsDNA isotypes in U/ml

	Day 0		Day 30		Day 60		Day 90	
Group #	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
hBCMA-300	179	560	163	371	150	706	171	841
hBCMA-100	150	430	259	718	171	822	339	1031
hBCMA-30	377	592	297	458	401	664	424	601
FC.	149	371	234	283	384	331	432	351
PBS	308	292	439	311	247	576	720	467

Standard Deviation of the above means

	Day 0		Day 30		Day 60		Day 90	
Group #	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM
hBCMA-300	104	303	116	211	62	518	62	734
hBCMA-100	109	262	306	461	212	758	371	1225
hBCMA-30	363	455	281	430	305	606	421	400
FC.	68	160	150	93	391	151	233	237
PBS	311	73	474	152	247	370	870	327

Figure 35: Evaluation of B cell numbers at treatment day 60 from the12mg/kg (30 ug), 4mg/kg (100ug), and 1.3mg/kg (300 ug) dose of hBCMA-Fc groups along with the Fc and PBS control groups.

hBCMA-fc-300				hBCMA-100				hBCMA-FC-30			
Mouse#	%CD4	%CD8	%B220		%CD4	%CD8	%B220		%CD4	%CD8	%B220
1.0	16.3	11.0	16.4	5.0	26.1	14.9	10.1	9.0	2.5	6.9	10.3
2.0	24.1	11.1	11.6	6.0	21.1	11.3	10.6	10.0	13.2	5.2	23.4
3.0	18.2	7.4	9.9	7.0	24.6	13.3	8.3	11.0	15.9	6.4	29.2
4.0	25.4	13.3	13.1	8.0	20.0	11.3	13.4	12.0	14.8	7.6	31.5
x	21.0	10.7	12.8	x	23.0	12.7	10.6	x	11.6	6.5	23.6
sd	4.4	2.4	2.8	sd	2.9	1.7	2.1	sd	6.2	1.0	9.5
Fc				PBS							
33.0	7.0	8.1	25.4	37.0	16.9	8.3	15.5				
34.0	10.7	4.9	15.3	38.0	19.1	12.1	19.5				
35.0	18.9	9.3	21.0	39.0	7.1	3.4	17.5				
36.0	20.1	11.1	21.0	40.0	19.9	11.4	26.5				
x	14.2	8.4	20.7	x	15.8	8.8	19.8				
sd	6.4	2.6	4.1	sd	5.9	4.0	4.8				

Figure 36: Specific APRIL binding to Human Cell lines determined by FACS analysis

	APRIL binding
HT 29 Colon adenocarcinoma	+ + +
NCI 460 Lung carcinoma	+ + +
PC3 Prostate adennocarcinoma	+ +
C6 Glial carcinoma	+ +
Raji Burkitt lymphoma	+ + +
A20 Mouse B cell lymphoma	+ + +
U266BI Myeloma	+ + +
A435 Epidermoid carcinoma	--
A469 Kidney carcinoma	--
MDA-231 breast adenocarcinoma	--

Figure 37: Effect of APRIL ,BCMA-Fc and TACI-Fc trucated on U266BI cell proliferation

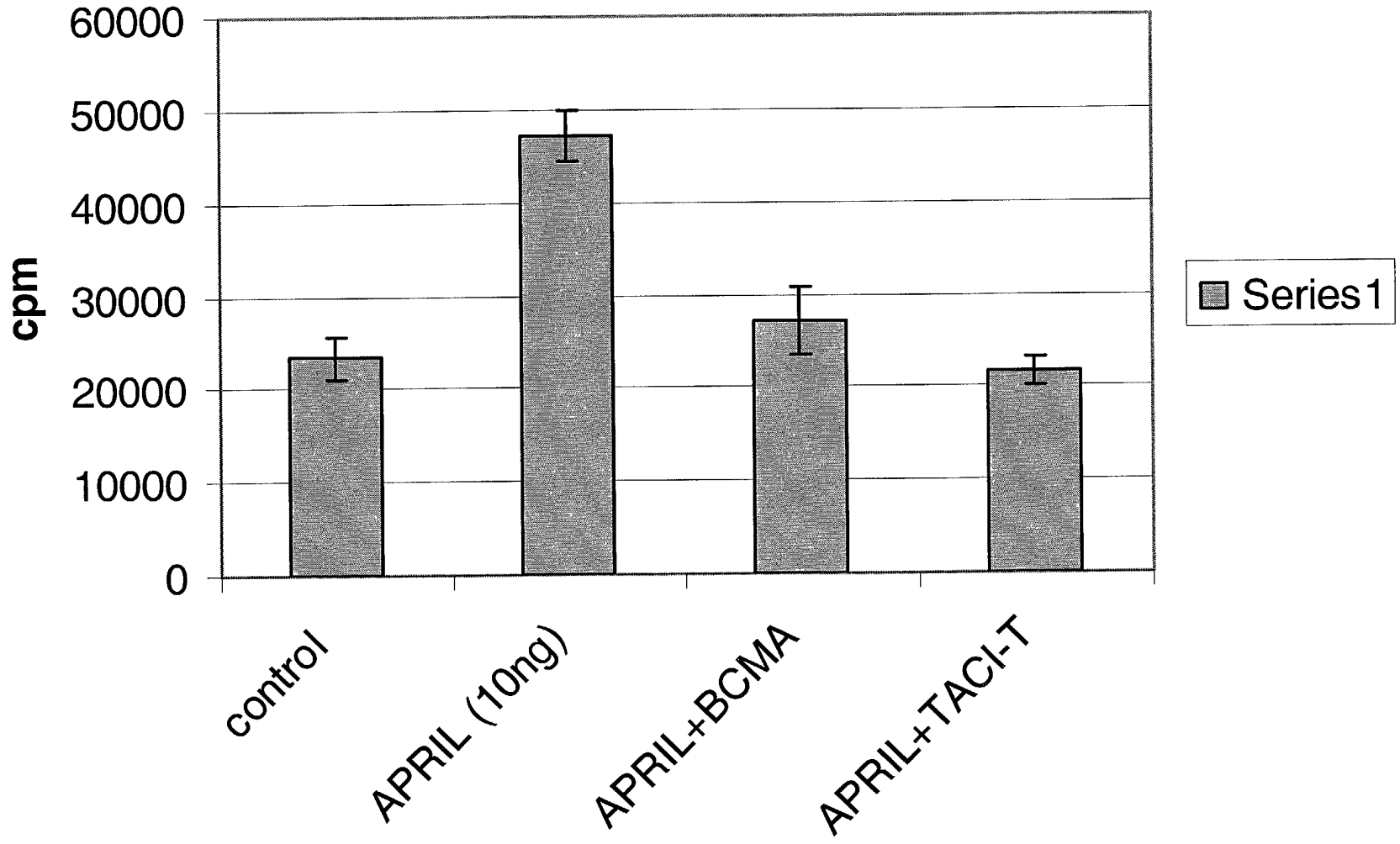


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Figure 38: APRIL and AGP3 stimulates and BCMA-Fc inhibits B lymphoma cell proliferation

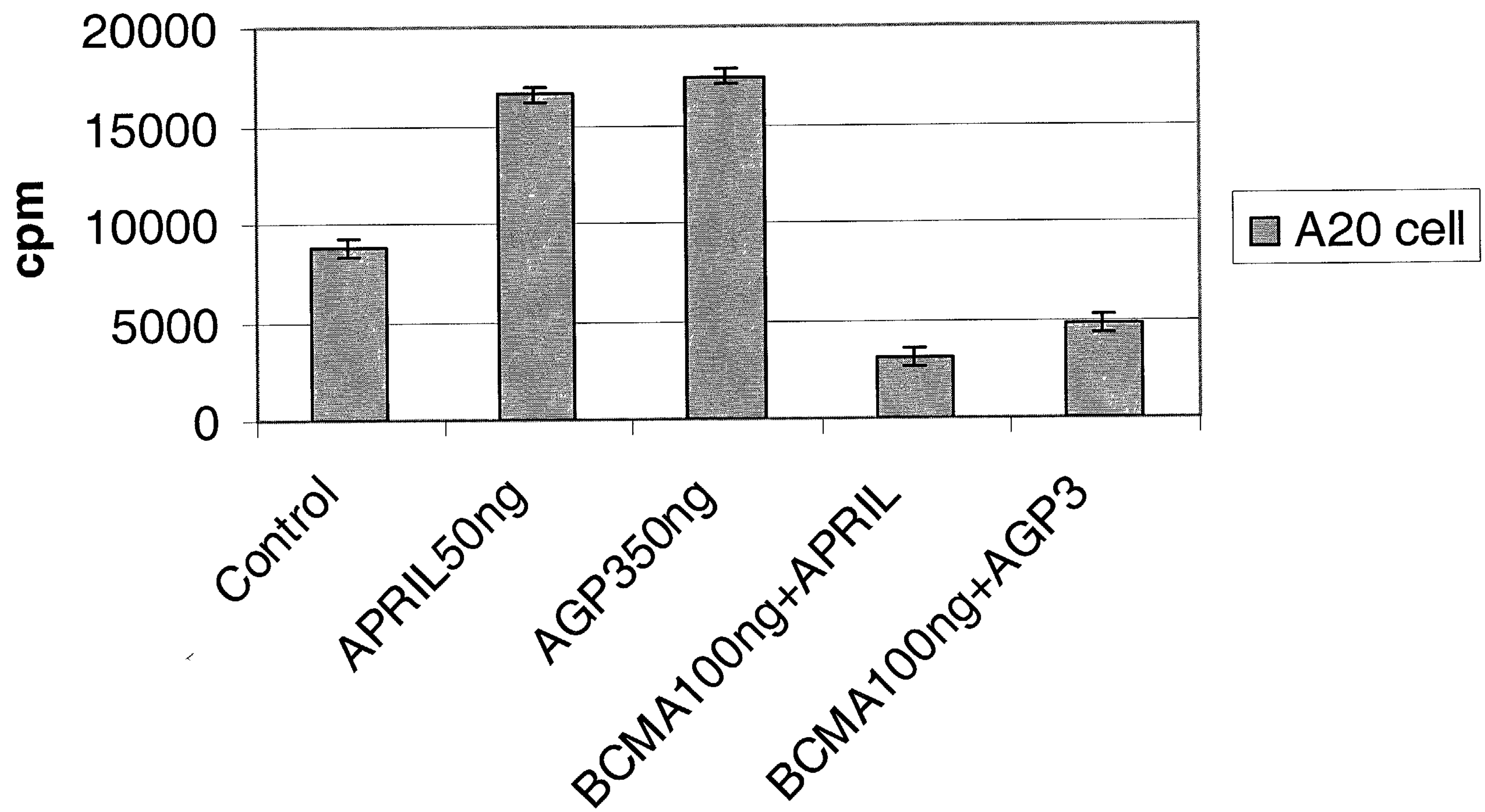


Figure 39: Effects of BCMA & hTACI on the Growth of A20 in Balb/c Mice

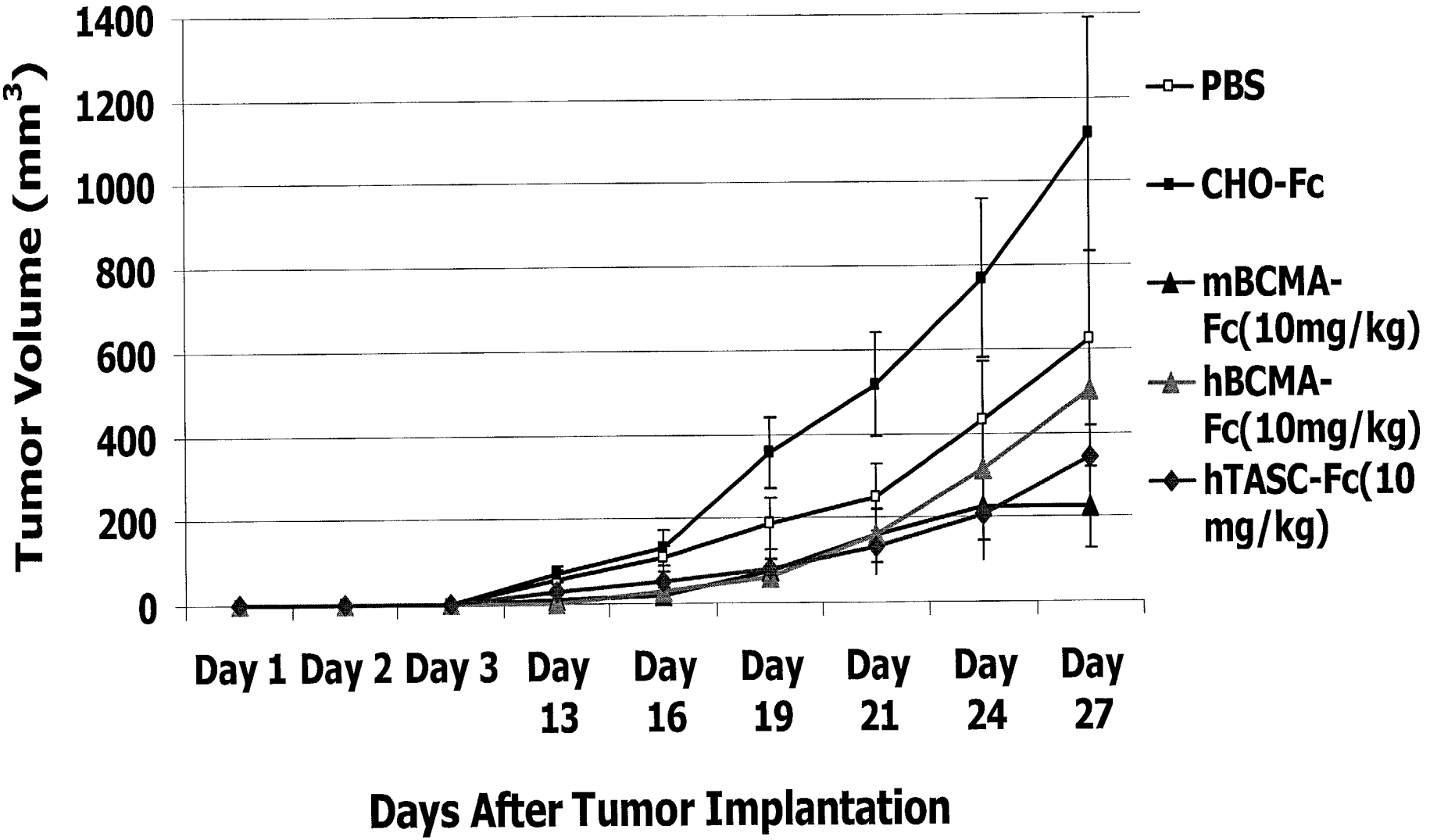
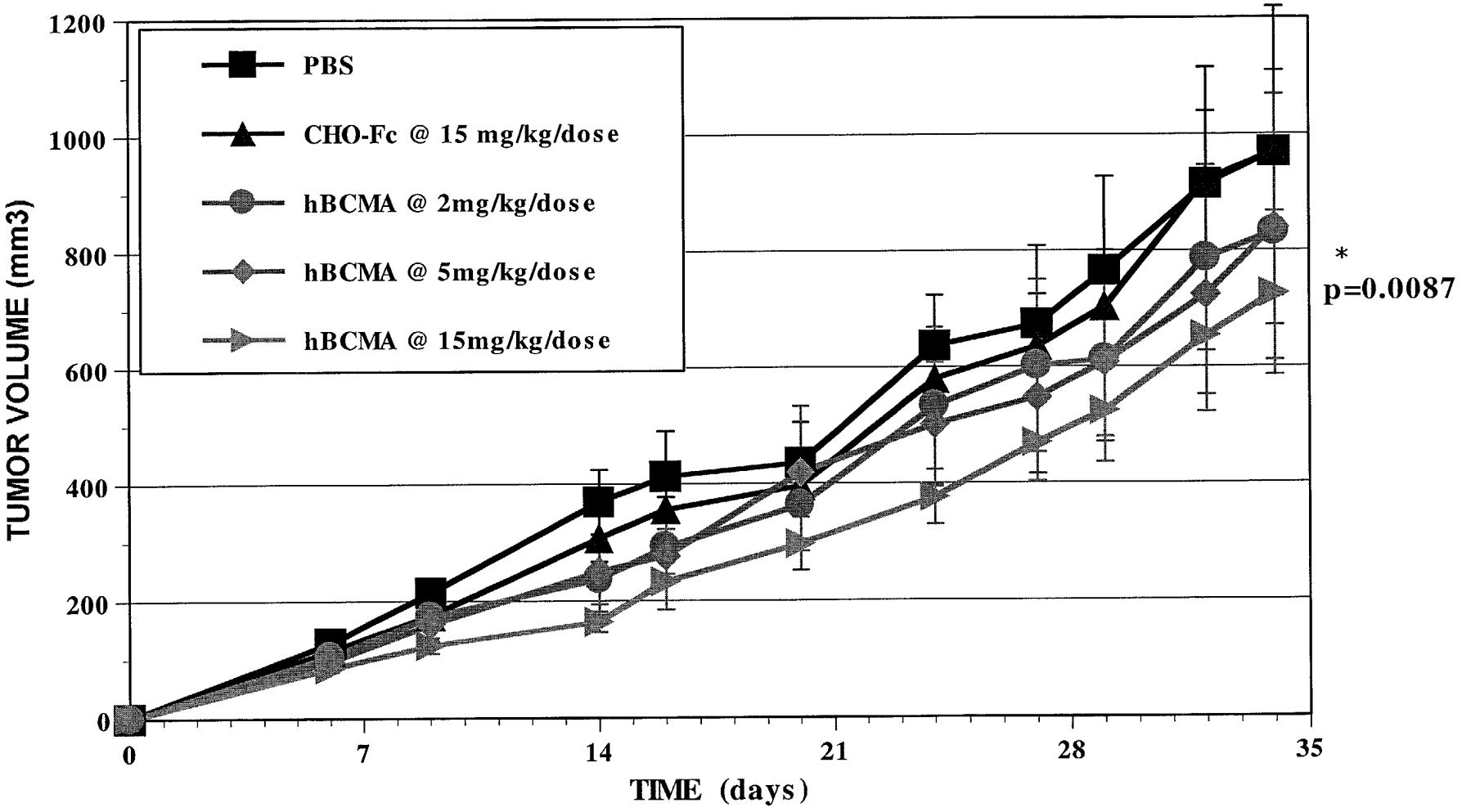


Figure 40

EFFECT OF HUMAN BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH

Rx: IP, Q2D, day 0

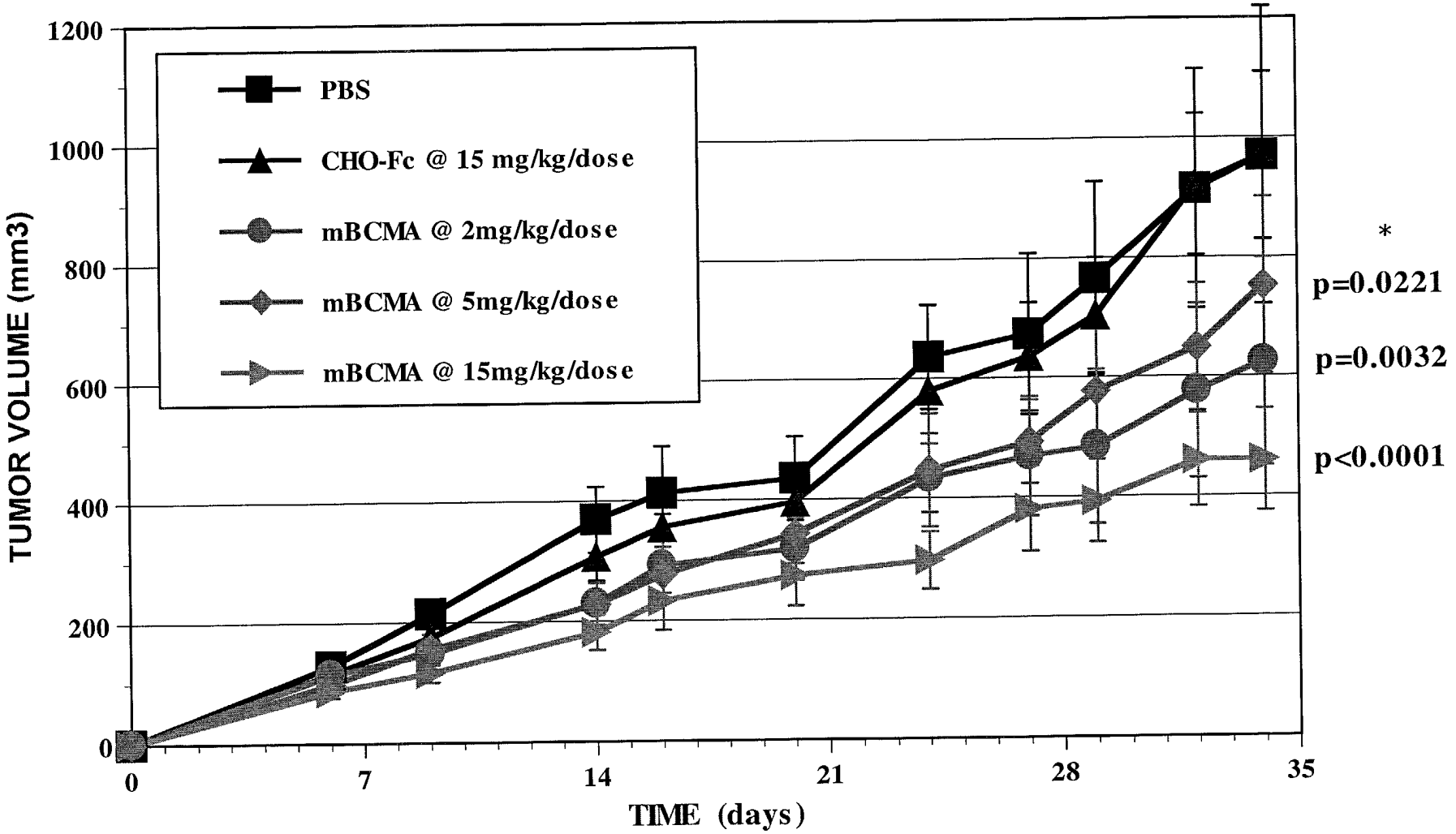


* Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)

Figure 41

EFFECT OF MURINE BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH

Rx: IP, Q2D, day 0



* Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)